ACCURACY OF COMPUTED TOMOGRAPHY FOR COMMON NEUROLOGICAL DISEASE IN HIV PATIENTS AT SIRIRAJ HOSPITAL

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Thesis
entitled

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ACCURACY OF COMPUTED TOMOGRAPHY FOR COMMON NEUROLOGICAL DISEASE IN HIV PATIENTS AT SIRIRAJ HOSPITAL

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ABSTRACT

Our study has collected CT brain images of 139 HIV patients in Siriraj hospital since 2008 to 2013. We used the image data of CT brain in pre-contrast and post-contrast for diagnosis common neurological disease in HIV patients. The accuracy of the study was ensured by using data correlation between imaging and blood histochemistry laboratory data. The accuracy of Computed Tomography was calculated for sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV). The study population included of 93 male and 46 females. The patients' age ranged from 10 to 71 years. Common neurological disease in HIV patients were Cryptococcal meningitis (46 patients, 32.6%), followed by Tuberculous meningitis (45 patients, 32.4%), HIV encephalopatchy or HIVE (37 patients, 26.6%), Toxoplasmosis (20 patients, 14.4%), Progressive multifocal leukoencephalopathy or PML (13 patients, 9.4%), Primary CNS Lymphoma or PCNSL (9 patients, 6.5%), Other (Brain metastasis, Intracerebral hemorrhage, Meningitis and Kaposi sarcoma) (5 patients, 3.6%), Tuberculomas (4 patients, 2.9%), and Cryptococcomas (3 patients, 2.2%), respectively. The Accuracy of common neurological disease was 68.3, 74.1, 56.8, 89.0, 93.5, 97.8, 96.4, 92.8 and 96.4 respectively. CT was found the most accuracy to have sensitivity, specificity, PPV and NPV for PCNSL (77.8%, 99.2%, 85.7% and 98.5%), respectively.

Cryptococcal meningitis, Tuberculous meningitis and HIVE were common neurological diseases to have high prevalence in HIV patients. The most accuracy of CT was showed with space occupying lesion such as PCNSL, PML, Toxoplasmosis, Tuberculomas and Cryptococcomas followed by Cryptococcal meningitis, Tuberculous meningitis and HIVE.

KEY WORDS: COMPUTED TOMOGRAPHY / COMMON NEUROLOGICAL-DISEASE / HIV PATIENTS

74 pages

การศึกษาความถูกต้องของภาพถ่ายเอกซเรย์คอมพิวเตอร์จากโรคทางระบบประสาทของผู้ป่วยเอชไอวีที่ได้เข้ารับการวินิจฉัยที่โรงพยาบาลศิริราช

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บทคัดย่อ

การศึกษานี้เป็นการศึกษาย้อนหลังในการเก็บข้อมูลผู้ป่วยเอชไอวีจำนวน 139 คน ที่เข้ารับการวินิจฉัยที่โรงพยาบาลศิริราชตั้งแต่ปี พ.ศ. 2551-2556 ซึ่งจะทำการศึกษาลักษณะและสาเหตุความผิดปกติของสมองที่พบในภาพเอกซเรย์คอมพิวเตอร์ โดยให้รังสีแพทย์ 2 ท่านแปลผลภาพถ่ายเอกซเรย์ก่อนโดยไม่ทราบข้อมูลเก่าจากเวชระเบียนจากนั้นจะนำผลการอ่านภาพถ่ายมาเปรียบเทียบกับผลการวินิจฉัยจากห้องปฏิบัติการเพื่อสรุปหาสาเหตุที่แท้จริงและนำไปสู่การพิจารณาความถูกต้อง (accuracy) ของแต่ละสาเหตุจากการประเมินค่า sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV)

จากภาพเอกซเรย์คอมพิวเตอร์ของผู้ป่วยเอชไอวีประกอบไปด้วยเพศชายจำนวน 93 คนและเพศหญิงจำนวน 46 คน โดยมีอายุอยู่ในช่วง 10-71 ปี ซึ่งผู้ป่วยเอชไอวีทั้งหมดได้รับการวินิจฉัยว่าเป็น Cryptococcal meningitis จำนวน 46 คน หรือ คิดเป็นร้อยละ32.6, Tuberculous meningitis จำนวน 45 คน หรือ คิดเป็นร้อยละ32.4, HIVE จำนวน 37 คน หรือ คิดเป็นร้อยละ26.6, Toxoplasmosis จำนวน 20 คน หรือ คิดเป็นจำนวน14.4, PML จำนวน 13 คน หรือ คิดเป็นร้อยละ9.4, PCNSL จำนวน 9 คนหรือคิดเป็นร้อยละ6.5, อื่นๆ ประกอบด้วย Brain metastasis, Intracerebral hemorrhage, Meningitis and Kaposi sarcoma จำนวน 5 คนหรือคิดเป็นร้อยละ3.6,Tuberculomas จำนวน 4 คนหรือคิดเป็นร้อยละ2.9 และCryptococcomas จำนวน 3 คนหรือคิดเป็นร้อยละ2.2 โดยค่าความแม่นยำของแต่ละโรคคือ 68.3, 74.1, 56.8, 89.0, 93.5, 97.8, 96.4, 92.8 และ 96.4 ตามลำดับ

โรค Cryptococcal meningitis, Tuberculous meningitis และ HIVE พบได้มากที่สุดในกลุ่มผู้ป่วยเอชไอวีจำนวน 139 คน โดยค่าความแม่นยำส่วนใหญ่แล้วจะอยู่ในกลุ่มของ spaceoccupying lesion เช่น PCNSL, PML, Toxoplasmosis, Tuberculomas, Cryptococcomas และ Cryptococcal meningitis, Tuberculous meningitis และ HIVE

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LIST OF ABBREVIATIONS

Abbreviations	Term
AIDS	Acquired Immune Deficiency Syndrome
BBB	Blood brain barrier
CT	Computer tomography
CNS	Central nerve system
CSF	Cerebrospinal fluid
CMV	Cytomegalovirus
CDC	Centers for disease control
CE	Contrast enhancement
DNA	Deoxyribonucleic acid
EBV	Epstein-Barr virus
FP	False positive
FN	False negative
HIV	Human immunodeficiency virus
HIV-1	Human immunodeficiency virus type 1
HIV-2	Human immunodeficiency virus type 2
HIVE	HIV encephalopathy
HSV	Herpes simplex virus
ICD 10	International classification of diseases and related health problem 10^{th} revision
IgG	Immunoglobulin G
IgM	Immunoglobulin M
JCV	John Cunningham virus
K	Kappa test
LTNPS	Long term nonprogressors
MRI	Magnetic Resonance Imaging

LIST OF ABBREVIATIONS (cont.)

Abbreviations	Term
NCE	Non contrast enhancement
NPV	Negative predictive value
NHLS	Non-Hodgkin's Lymphoma
NO.	Number
PML	Progressive multifocal leukoencephalopathy
PCNSL	Primary CNS Lymphoma
PCR	Polymerase Chain Reaction
PET	Positron emission tomography
PCP	Pneumocystis pneumonia
PPV	Positive predictive value
SPECT	Single photon emission computed tomography
TBM	Tuberculous meningitis
TB	Tubercle bacillus
T.gondii	Toxoplasma gondii
TP	True positive
TN	True negative
UNAID	United States Agency for International Development-USAID
WM	White matter

CHAPTER I
INTRODUCTION

The human immunodeficiency virus (HIV) is a retrovirus that infects cells of the immune system and destroys or disrupts their function. In the more advanced stages of HIV infection, it will be developed to acquired immunodeficiency syndrome (AIDS). The World Health Organization reported that there were 31.4-33.5 million AIDS-patients worldwide in 2006. In 2008, AID was the problem 6th of all disease and found the mortality about 1.78 million people worldwide. The last report in 2012 estimated more than 35.3 million people worldwide.

In Thailand, there were 372,874 people of all AIDS-patients and were died 98,153 people in September 1984 to December 2011. The age of patients ranged from 5 to 60 years and the most age of 25 to 40 years (1).

The Central Nervous System (CNS) is the most target of the human immunodeficiency virus (HIV). HIV can lead to CNS by crosses the blood brain barrier (BBB) at an early stage of the disease. Up to 60% of AIDS patients will have neurologic manifestation which will be the first clinical manifestation of AIDS patients about 10% of cases (2). Common neurological diseases are classified into direct infection and indirect infection. The direct infection is result from HIV- itself includes HIV encephalopathy (HIVE) that caused AIDS-dementia, becoming the most frequent neurologic complication of HIV infection. The indirect infections are opportunistic infection and malignancies include Toxoplasmosis, Cryptococcal meningitis, Cryptococcomas, Tuberculous meningitis, Tuberculomas, Progressive multifocal leukoencephalopathy (PML) and Primary CNS lymphoma (PCNSL) (3).
Diagnosis based on the history, characteristic manifestations, the results of laboratory tests and radiologic findings. Characteristic manifestations may be showed by each the disease that include Meningitis pattern presents fever, headache, stiff neck, vomiting, blurred vision such as Cryptococcal meningitis, Tuberculous meningitis. Encephalitis presents fever, headache, confused, seizure and weakness. Brain abscess presents

weakness, seizure, headache and confuse such as Toxoplasmosis, Tuberculomas and Cryptococcomas. Brain tumor presents rapid progression of confusion, lethargy, memory loss, focal neurology and seizures such as PCNSL. Headache will be presented the first symptom of common neurological disease (4).

Laboratory presentation in HIV-patients was showed anti-HIV, Standard test for Cerebrospinal fluid (CSF) include CSF protein, sugar and cell count but the tests are nonspecific. Although, CSF-antigen, Polymerase chain reaction (PCR), and CSF culture have high specificity, but low sensitivity. In addition, brain biopsy is an invasive procedure and risk for personnel. This procedure is limited.

The CD4+ T lymphocytes are the best predictor at all stages of diseases. The patient is immunity weak when the CD4 counts <200 cells/mm^3. Immunological staging of HIV are most frequently defined: <200 cells/ mm^3, 200-500 cells/ mm^3 and ≥500 cells/mm^3. Most CD4-count is <200 cells/ mm^3 include HIVE, Cryptococcal meningitis, Toxoplasmosis, PCNSL and PML (5). As clinical symptoms may be nonspecific and laboratory testing is often unhelpful. Nevertheless, radiological interpretation still relies for diagnosis, the exclusion of occult pathology and follow up, and monitoring of therapy. As CT is a choice for diagnosis, even though, its sensitivity of lesion detection has not the same as MRI. However, CT has various advantages such as low cost, safe and more widespread, whereas other imaging modalities i.e. Magnetic Resonance Imaging (MRI), Single-Photon Emission Computed Tomography (SPECT), and Positron Emission Tomography (PET) but they are not widespread at the present.

CHAPTER II
OBJECTIVES

2.1 General objective

To evaluate a prevalence of common neurological disease, such as Cryptococcal meningitis, Tuberculous meningitis (TBM), HIV encephalopathy (HIVE), Toxoplasmosis, Progressive multifocal leukoencephalopathy (PML), Primary CNS lymphoma (PCNSL), Tuberculomas and Cryptococcomas in HIV patients at Siriraj hospital.

2.2 Specific objective

To evaluate accuracy of Computed Tomography (CT) for diagnosis common neurological disease in HIV patients at Siriraj hospital since 2008 to 2013. However, the study used the image data of CT brain in pre-contrast and post-contrast for diagnosis common neurological disease in HIV patients. Accuracy of study was done by using data correlation between imaging and blood histochemistry laboratory data. The accuracy of CT was calculated for sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV).

CHAPTER III
LITERATURE REVIEWS

3.1 Background and rationale

Human immunodeficiency virus (HIV) is a virus in group of "family Retroviridae", being a big family that compose many virus. The most host of the family is Vertebrae. HIV can highly mutate owing to more division of itself. It can divide within human's cells such as white blood cells and brain cells. Therefore, if the body cannot fight, it will have a weak immune. As a result, HIV patient can become AIDS patient.

Human retroviruses is divided into 2 types including human immunodeficiency virus type1 (HIV-1) and human immunodeficiency virus type2 (HIV-2). HIV-1 was found in Africa, USA, Europe, Western of Pacific and Asia. Another type is found in Western of Africa. However, HIV-2 will be found less many violence pathogens than HIV-1 (6).

The first case of AIDS patients was found at the United States between 1980 and 1981. Dr. Michael Gottleib and team (6) found the five men who were pneumonia caused by Pneumocystis carinii (PCP). Moreover, they are found cytomegalovirus (CMV), candida. Those diseases are usually found in immunodeficiency. Furthermore, the interesting same characters of all men are 29-36 years old, a strong man and a homosexual. However, the disease can usually contact from a person to a person. Therefore, it is called "acquired immunodeficiency syndrome (AIDS)". For Thailand, the first case of the AIDS patients is a 28 years old man, which studied in USA. Furthermore, he is also a homosexual. In 1983, he had been examined and treated which found that he was pneumonia caused by Pneumocystis carinii (PCP). Finally, he was AIDS and died (7). Therefore, AIDS were the principal cause of morbidity and mortality in the patients with HIV infection.

The United States Agency for International Development-USAID (UNAID) reported from 143,000 AIDS patients to 9,700 people in 1991 to 2011. In

2011, there were 490,000 people living with HIV and 23,000 people died by AIDS-related illnesses (8).

In 2012, there were 35.3 million people worldwide. The new patients were 2.3 million people and died 1.6 million people decreasing from 2005 about 30% owing to using HAART.

Epidemiological information section Bureau of Epidemiology, Department of Disease Control, Ministry of publish health in Thailand reported that there were 372,874 AIDS patients in 1984-2011. A number of AIDS patients were died 98,153 people. They are 20-44 years old. The most of age was 30-34 years old (24.94%), followed by 25-29 years old (21.74%), 35-39 years old (18.09%), 40-44 years old (10.57%) and 10-14 years old (0.43%) (9). UNAID speculated that 1.2 million people in 2013. The new patients were 8,959 people. The most of age was 30-34 years old. The most of cause was sexual (84.26%), followed by injecting drug (4.36%) and infection from mother (3.53%).

3.2 Stage of HIV infection

HIV infection is divided 3 stages (6) which include:

3.2.1 Typical progresses

The HIV patients will present a symptom and become AIDS patients within 8-10 weeks after infection. There is about 80-90%. It is divided 4 stages.

3.2.1.1 Primary infection

Most of the patients may be asymptomatic in this stage. Nevertheless, some patient may present a symptom within 3-6 weeks after infection. The symptoms are fever, sore throat, lymphadenopathy, fatigue and headache etc. However, the stage cannot detect antibody but blood can find more virus. Therefore, these patients are serious enough to consult a doctor. However, this stage cannot diagnose.

3.2.1.2 Clinical latency

This stage will present a symptom within 5-10 years after infection. They are a carrier. The stage has decrease of CD4 lymphocytes. Therefore, the diagnosis can detect owing to discovery of more virus.

3.2.1.3 Symptomatic HIV infection

This stage will present a symptom within 8-10 years after infection. Most of the symptoms are high fever (37.8^{o} C), chronic diarrhea, weigh loss more than 10% of weight body etc. There are a decrease of number CD 4+lymphocytes. Therefore, the stage is mainly cause of opportunistic infection which leads to weak immune system.

3.2.1.4 Acquired immunodeficiency syndrome (AIDS)

AIDS diagnosis is confirmed when the patient with HIV infection is developed by opportunistic infections or cancers.

3.2.2 Rapid progressors

This stage becomes suddenly AIDS. The patients with HIV present a symptom within 3-4 years after infection. There is about 10-15%.

3.2.3 Long term nonprogressors (LTNPS)

The patients with HIV infection present asymptomatic more than 8-10 years after infection. There is about 5-10%. Moreover, the patient may have CD4 count > 500 cells/mm^3.

3.3 The important target of HIV

The most target of HIV is helper T lymphocytes, which is primary target cell. The surface of target cell has a CD4 molecule that is called CD4+ lymphocyte. They have been an important marker for predict a disease staging, the relative risk of developing opportunistic infections or neoplasm and follow a patient who is treated with antiretroviral therapy (HAART). However, testing for number CD4+ lymphocyte

may be shown an absolute number (cell/mm^3) or percentage. They are shown by the U.S. Centers for Disease Control (CDC).

Table 3.1 The absolute number of CD4 lymphocytes and its prediction

Absolute number of CD4+ T cells	Prediction
> 500 cells/mm^3 or 29%	Normal immunity
200-499 cells/mm^3 or 14-28%	Rather weak immunity
< 200 cell/mm^3 or <14%	Few weak immunity

3.4 HIV-related neurological disease

The central nervous system (CNS) is the important target of the Human deficiency virus (HIV), which can cross blood–brain barrier (BBB) at an early stage. BBB is preventing foreign bodies through into the brain and spinal cord. Therefore, all kind of infections cause the BBB to break down and result to abnormal of the brain such as brain dementia, brain abscess, and brain meningitis and brain tumor. These are causes significant of morbidity and mortality in AIDS patients.

CNS complication of AIDS patients occur about 10 % of cases and 40-80% of AIDS patients presenting neurologic manifestations (10). Most of the neurologic manifestations are headache, dementia, confusion and loss memory.

HIV-related neurological disease is classified into primary infection and secondary infection. The primary infection is caused by HIV itself such as AID-dementia, aseptic meningitis, HIV-related seizure and distal symmetric sensory polyneuropathy. The secondary infections include opportunistic infections and malignancies such as lymphoma.

Table 3.2 Neurological complications of HIV infection (11).

Primary infection	Secondary infection
HIV dementia	Toxoplasmosis
Vacuolar myelopathy	Progressive multifocal leukoencephalopathy (PML)
Cerebrovascular disease	Primary CNS lymphoma (PCNSL)
Inflammatory demyelinating polyneuropathy	Cryptococcus neoformans infection
Aseptic meningitis	Cytomegalovirus encephalitis
Distal symmetrical polyneuropathy	Cytomegalovirus polyradiculopathy
Mononeuritis multiplex	Tuberculous meningitis
Myopathy	Aspergillus infection

The commonest of neurological diseases in HIV infection (10) were HIV encephalopathy, Toxoplasmosis, Primary CNS lymphoma, PML and Cryptococcosis followed by Mycobacterium, Candida, Cytomegalovirus and Herpes simplex. Nevertheless, Candida, Cytomegalovirus and Herpes simplex were found as a few diseases in Thailand. The Epidemiological information section Bureau of Epidemiology, Department of Disease Control, Ministry of publishes health reported in 1984 – 2012.

There were Mycobacterium tuberculosis 112,315 people (30.12%), Cryptococcosis 50,304 people (13.49%), Toxoplasmosis 10,856 people (2.91%), HIV encephalopathy 4,785 people (1.28%), primary CNS lymphoma 1,313 (0.35%) and PML 323 people (0.09%). Therefore, those diseases are mostly found in the HIV patient of Thailand.

3.5 Incidence of neurological diseases in Thailand.

3.5.1 The report of Ramathibodi Hospital (2001-2005)

Keerati Hongsakul MD and Jiraporn Laothamatas MD (12) studied HIV Patients at Ramathibodi Hospital since January 2001 and December 2005. The study was retrospective study which had all total 195 patients that included of 114 males and 81 females. The mean age was 34 years (range 21-77 years). The most of CNS infection was HIV encephalitic 59 %, followed by Toxoplasmosis 22%, Cryptococcomas 9%, Tuberculous meningitis 5%, Tuberculomas 4%, Progressive multifocal leukoencephalopathy (PML) 3%, Lymphoma 2 %, and normal 1 %, Meningitis pattern 33%, Infarction 5% and Cerebritis 4 %.

3.5.2 The report of Nonghan Hospitalsince (2008-2010)

PreechaSrisrangthong (13) studied the retrospective study of HIV Patients at Nonghan Hospitalsince 2008 to 2010. The study was retrospective study which had all total 220 patients that included of 112 males and 108 females. All 92 patients were opportunistic infection. There were 58 males and 34 females. Forty-eight patients (52.17%) were aged 31 to 40 years, followed by 19 patients (20.65%) were aged 21 to 30 years, 14 patients (15.22%) were aged 41 to 50 years and 7 patients (7.69%) were aged 51 to 60 years. The most of opportunistic infection was Pulmonary TB 42 patients (45.65%), followed by PCP 23 patients (25%), Cryptococcal Meningitis 16 patients (17.39%), extra pulmonary TB and Disseminated TB 6 patients (6.52%), CMV 2 patients (2.17 %), Toxoplasmosis 2 patients (2.17 %), and MAC 1 patients (1.09 %).

3.5.3 The report of King Chulalongkorn Memorial Hospital (2010-2012)

Siriporn Kongsiriwattanakul MD and Chusana Suankratay MD, PhD (14) studied HIV Patients at King Chulalongkorn Memorial Hospital by identified from The International Classification of Disease (ICD 10) since 1 January 2010 to 31 December 2012. The study was retrospective study which had all total 148 patients that included of 103 males and 45 females. The mean age of 36.1 + 8.9 years (range 15

to 75 years).The most of CNS infection was Cryptococcus neoformans 56 patients (37.8 %), followed by Tuberculosis 53 patients (35.8%), Toxoplasmosis 19 patients (12.8%), Progressive multifocal leukoencephalopathy 6 patients (4.1%),Meningitis from Varicella-zoster virus (VZV) 4 patients (2.7%), Brain abscess 3 patients(2.1%), Cytomegalovirus(CMV) 2 patients (1.4%), Meningitis from Streptococcus pneumonia 2 patients (1.4%), Encephalitis from Herpes simplex virus (HSV) 1 patients (0.7%), and Primary CNS lymphoma 1 patients(0.7%).

3.6 Clinical manifestations of HIV-associated with CNS infection in Thailand

3.6.1 The report of King Chulalongkorn Memorial Hospital (2010-2012)

Siriporn Kongsiriwattanakul MD and Chusana Suankratay MD, PhD (14) reviewed all 148 patients with CNS infection, the most common presenting neurological symptom was headache (97 patients, 65.5%), followed by altered consciousness (52 patients, 35.1%), nausea/vomiting (52 patients, 35.1%), weakness (35 patients, 23.6%), seizures (32 patients, 21.6%), diplopia (10 patients, 6.8%), blurred vision (10 patients, 6.8%), and numbness (8 patients, 5.4%). The most of extra-neurological symptom was fever (86 patients, 58.1%), followed by cough (16 patients, 10.8%), dyspnea (9 patients, 6.1%), chills (8 patients, 5.4%), diarrhea (8 patients, 5.4%), abdominal pain (4 patients, 2.7%), skin rash (4 patients, 2.7%) and others (14 patients, 9.5%).

3.7 Neurological diseases

3.7.1 Primary infection

3.7.1.1 HIV encephalopathy or HIVE (15)

3.7.1.1.1 Epidemiology

The primary infection of CNS is HIV encephalopathy (HIVE) causing of AIDS-dementia or subcortical dementia. HIVE occur later stages of HIV infection. The incidence of HIVE is about 10-30% of AIDS patients. Most of the cases are observed in a patient who have CD4-counts < 200 cells/mm^3.

3.7.1.1.2 Clinical manifestation

The patient with HIVE often showed more violence of symptom when compound with another opportunistic infection or mimic with dementia. Therefore, the diagnosis of HIVE can examine when mimic of dementia has improved. Generally, the patient with HIVE occasionally showed symptom that upon history of an individual patient. Most of the symptoms present slowing of reasoning, forgetfulness, difficulties concentrating, lack of energy drive, mild depressive symptoms and emotional blunting. However, impairment of alertness neck stiffness and focal or hemiparesis, aphasia cannot diagnose with HIVE. Seizures are rarely showed with HIVE.

3.7.1.1.3 Diagnosis

The diagnosis of HIVE must have a result of both clinical manifestation and laboratory test. For clinical manifestations were mentioned. Laboratory test determined with CSF showed a normal or decrease of white blood cell and concentration of protein and albumin slightly decrease. Nevertheless, it is non-specific test and cannot identify with HIVE.

Therefore, radiology instrument, including CT and MRI, are used to diagnose. Although, MRI is better instrument than CT but CT is often used in many hospitals. The characteristic of CT is mentioned in title 3.8.

3.7.2 Secondary infection

3.7.2.1 Cryptococcal meningitis and Cryptococcomas (16)

3.7.2.1.1 Epidemiology

Cryptococcus neoformans (C. neoformans) or Cryptococcosis is the commonest opportunistic infection associated with HIV. It is an encapsulated fungus, which is found in the soil contaminated by bird excrement. It can transmit into human by inhalation and localized disease in the lung and dissemination into the brain, leading to the development of Cryptococcal meningitis and Cryptococcomas. The incidence of Cryptococcus infection is about 10% of AIDS patients (17). Cryptococcus infection is usually asymptomatic because the body can be damage the infection but will show symptoms in the people with immunocompromised such as AIDS patients. Cryptococcus infection is the third most common cause of CNS infection in AIDS patients. Most of the cases are observed in patients who have CD4-counts < 100 cells/mm^3.

3.7.2.1.2 Clinical manifestations (17)

The symptoms of Cryptococcus infection were presented type of infection. Therefore, meningitis and meningoencephalitis present with fever, malaise, and headache. However, meningeal symptoms present neck stiffness and photophobia, occuring about 25-33% of patients. Moreover, encephalopathic symptoms present lethargy, altered mentation, personality changes, and memory loss, causing increased intracranial pressure because of CSF absorption or infection in brain.

3.7.2.1.3 Diagnosis

Cryptococcus neoformans can diagnose with culture of blood or CSF. Both 55% of all patients with blood culture and 95% of all patients with CSF culture are positive and can be detected within 7 days. Moreover, india ink of CSF can also shows encapsulated yeast in 60 - 80% of cases. Furthermore, CSF of cryptococcal antigen (Cr Ag) is also positive in meningoencephalitis and serum of Cr Ag is positive both meningeal and non-meningeal. However, the antigen

of blood or CSF is a useful initial screening tool in diagnosis. Moreover, it may also be useful for lumbar punctures are rejected. Testing for opening pressure of CSF may be found with pressure ≥25 cm H_2O occurring in 60-80% of all patients. Also radiology instrument are used to diagnose that is mentioned in title 3.8.

3.7.2.2 Tuberculous meningitis and Tuberculomas

3.7.2.2.1 Epidemiology

Tuberculosis (TB) is a serious disease that caused by the bacteria infection is called "Mycobacterium tuberculosis" (M.tuberculosis). It can occur in the early stages of HIV infection. However, it can contact from person to person by coughs, sneezes, speaks, or sings. Tuberculosis is about to spread through the air. If they take air containing TB, they will become the patient with TB. The most of TB infection affect the lungs, followed by other parts of the body, such as the central nervous system (CNS), which are cause of Tuberculosis meningitis (TBM) and Tuberculomas However, AID patients, who have higher many incidences than in the normal patient. The incident of CNS infection can occur in 5-10% of TB patients with HIV infection which are compared with 2-5% of TB patients without HIV infection (18). The patients are CD4–counts < 200 cells/mm^3.

3.7.2.2.2 Clinical manifestation

The most common of Tuberculous meningitis (TBM) include headache, fever, malaise, confusion, weight loss, seizures and meningism.

3.7.2.2.3 Diagnosis (19)

Diagnosis of Tuberculosis is considered clinical manifestation, characteristic radiology finding and the results of laboratory tests. However, a chest x-ray may provide significant in the first diagnosis of CNS with TB. As AIDS patients with TB will have an abnormal of chest radiography. CSF cannot always occur and culture of TB take up to 6-8 weeks. Therefore, CT is an important role for diagnosis that is mentioned in title 3.8.

3.7.2.3 Toxoplasmosis

3.7.2.3.1 Epidemiology

Toxoplasmosis is a disease caused by a parasite called “Toxoplasma gondii” (T.gondii), which has been found all warm-blooded animals including cats, pets and humans. HIV-patients are acquired from contact with cat or cat feces. The human will be acquired by inhalation, blood transfusion from an infected person, eating raw or undercooked meat. The report was found about 50-80% of HIV-patients in Europe, compared with 30% in the UK. Because of the area of Europe is warm area with high rainfall where the parasite is more likely to survive. The infection is the most common cause of focal brain lesions in 3-40% of patients when patients was advanced by HIV infection and CD 4 counts < 200 cells/mm^3. HIV-patients with CD4-counts <50 cells/mm^3 are at greatest risk (19).

3.7.2.3.2 Clinical manifestations (20)

As a result of clinical disease in AIDS patients with Toxoplasmosis infection belong to reactivation of the period infection. Commonest of disease is cerebral abscess which is the development of focal neurological signs and symptoms. However, the commonest of symptoms is headache that is a result of raises intracranial pressure, followed by confusion, fever, personality change. Some a patient may be altered levels of consciousness and seizures.

3.7.2.3.3 Diagnosis (10)

Toxoplasmosis is diagnosed based on the history, characteristic manifestations, radiologic findings and the results of laboratory tests. Measurement of anti-toxoplasma immunoglobulin G (IgG) and anti-toxoplasma immunoglobulin M (IgM) to T.gondii in the blood can diagnose toxoplasmosis but a low titer of antibody dose not exclude the diagnosis finding about 3% of patients are negative. Detection of PCR with toxoplasma DNA in CSF is a promising definitive diagnostic tool. Furthermore, the diagnosis of T.gondii may require with CT or MRI that is mentioned in title 3.8.

3.7.2.4 Progressive multifocal leukoencephalopathy (PML)

3.7.2.4.1 Epidemiology

A demyelinating disease caused by infection of oligodendrocyte with John Cunningham virus or JC virus, destroying oligodendrocyte and their myelin. The incidence of PML with AIDS patients is about 3%-7% of all patients and can be found in childrenhood and adults. Mortality rate comprised up to 18% of all patients. However, PML will be developed in patients with CD4-counts were range of 50-100 cells/mm^3 or some patients with CD4-counts of > 200 cells/mm^3.

3.7.2.4.2 Clinical manifestations

Clinical manifestation of PML (21) depends on location of the brain damage. There may be hemisphere, visual deficit which occur in up to 30%–50% of the patients with PML, speech defects, limb in coordination, motion deficit, preserved consciousness and without headache and fever.

3.7.2.4.3 Diagnosis

Diagnosis of PML is considered clinical manifestation, characteristic radiology finding and detection in CSF by PCR. However, testing of JCV DNA may be detected with cerebrospinal fluid (CSF) by Polymerase chain reaction (PCR) test, which its specificity was 92-100% and sensitivity was 72-92% (21). Furthermore, if PCR analysis is negative, lumbar puncture will repeat test. And brain biopsy is required to complete a diagnosis when JCV DNA in CSF is fail. Moreover, radiology instrument are used to diagnose that is mentioned in title 3.8.

3.7.2.5 Primary CNS lymphoma or PCNSL

3.7.2.5.1 Epidemiology

Primary CNS lymphoma (PCNSL) is a diffuse, large cell non-Hodgkin lymphoma of B-cell type. PCNSL is found less than 2% of central nervous system (CNS) tumors and 0.5–2% of all non-Hodgkin's lymphomas (NHLs) (1). The incidence of AIDS patient with PCNSL is about 5%. Furthermore, it can appear both HIV patients and non-HIV patients but the risk of HIV patients was more than in non-HIV patients. They may be CD4-counts < 100 cells/mm^3.

3.7.2.5.2 Clinical manifestations

The most of patients present with rapid progression of confusion, lethargy, memory loss, focal neurology and seizures but headache is uncommon.

3.7.2.5.3 Diagnosis

Diagnosis of PCNSL is considered clinical manifestation, characteristic radiology finding and the results of laboratory tests. Epstein-Barr virus (EBV) is the important virus of disease. As EBV DNA in CSF, which is detected by PCR test, has high sensitivity and specificity. However, CSF cytology is unhelpful. Furthermore, Brain biopsy is necessary to confirm the diagnosis. Moreover, radiology instrument are used to diagnose that is mentioned in title 3.8.

3.8. Computed Tomography for diagnosis

Clinical manifestations are non-specific. Laboratory test may be often unhelpful owing to distinguishing between stages of neurological disease become in AIDS. Although, Polymerase chain reaction (PCR) CSF analysis have developed the ability to make a specific diagnosis. Nevertheless, radiological interpretation still relies for diagnosis, the exclusion of occult pathology and follow up, and monitoring of therapy. As CT is a choice for diagnosis, even though, its sensitivity of lesion

detection has not the same as MRI. However, CT has various advantages such as low cost, safe and more widespread.

The important of diagnosis is overlap of imaging. Therefore, interpretation is essential. CT is a first line investigation. The interpretation is simply made by categorizing of each disease.

3.8.1 HIV encephalopathy (HIVE)

Osborn and team (22) reported CT finding of HIVE. CT typical reveal atrophy and symmetric, periventricular or diffuse white matter (WM) for distribution. However, non-contrast enhancement (NCE) shows normal or atrophy, diffuse white matter hypodensity and no mass effect. As contrast enhancement (CE) usually shows no contrast-enhancement. Moreover, MRI is used to detect of white matter because CT often missed for detection.

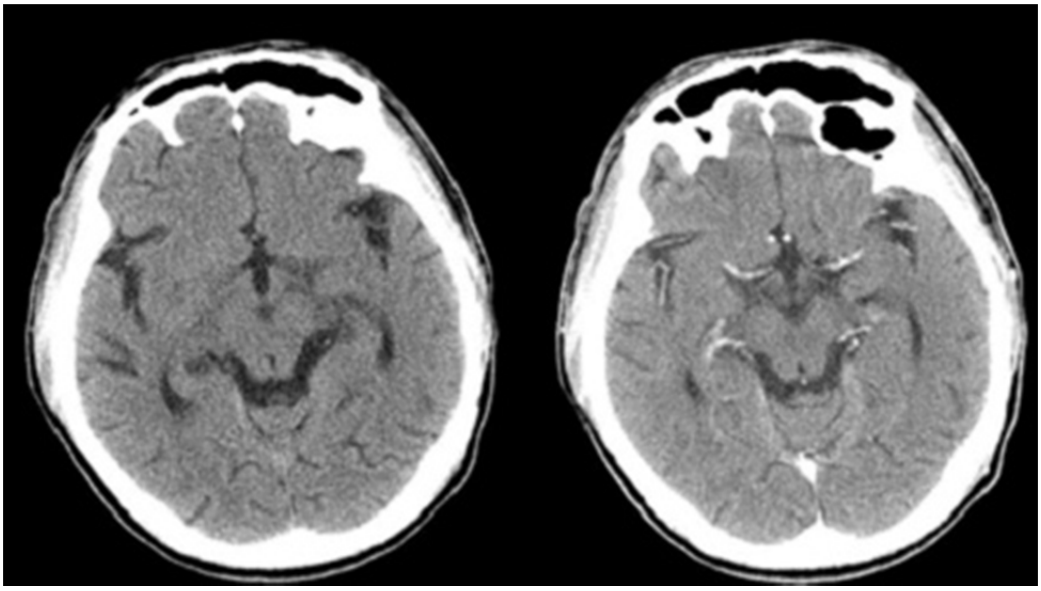


Figure 3.1 HIVE presented diffuse brain atrophy advance than age in 29 years old (12).

3.8.2 Progressive Multifocal Leukoencephalopathy (PML)

CT typically reveals single or multiple confluents, asymmetric focal and hypodense lesions without mass effect or edema. Contrast enhancement shows non-enhancement. However, location may find in the parieto-occipital white matter, basal ganglia, external capsule and posterior fossa.

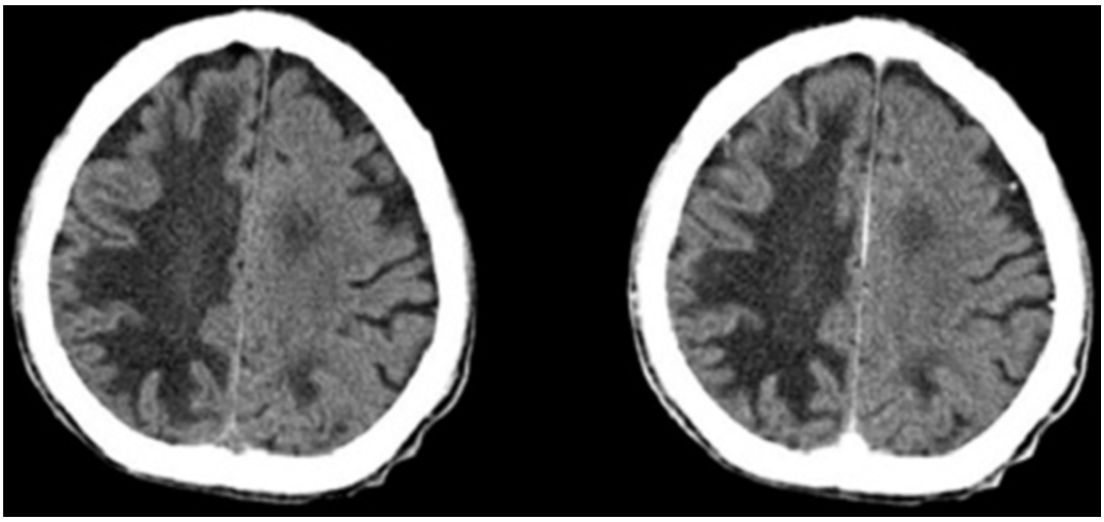


Figure 3.2 PML presented non-enhancing hypodense lesion involving right frontoparietooccipital and left parietal lobes without mass effect (12).

3.8.3 Cryptococcomas

Cryptococcomas may be found about 10% of the patient with cryptococcus infection. CT is seen a solid or ring enhancement parenchymal mass with surrounding edema and hydrocephalus. They may be an obstructive hydrocephalus because of arise within the choroid plexus (1).

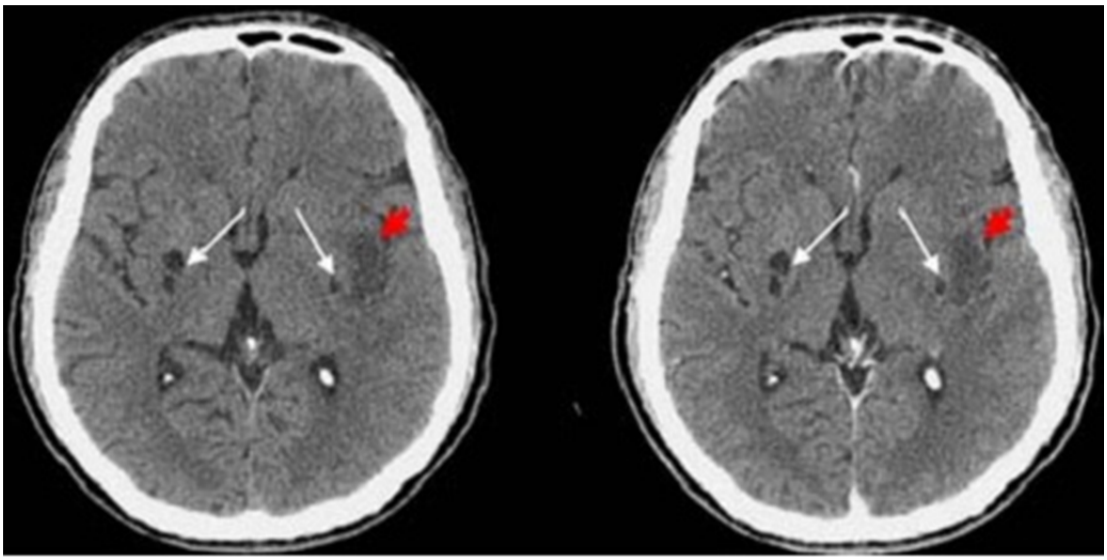


Figure 3.3 Cryptococcomas presented few non-enhancing well defined hypodense lesions at basal ganglia (arrows) representing cryptococcomas. Incidental subacute infarction is seen at the left insular cortex (arrowhead) (12).

3.8.4 Cryptococcal meningitis

CT typical reveals multiple nodular enhancements in the parenchyma and leptomeninges. It is rarely hydrocephalus and diffuse menigeal enhancement. In some patient may be shown normal scan on CT (19).

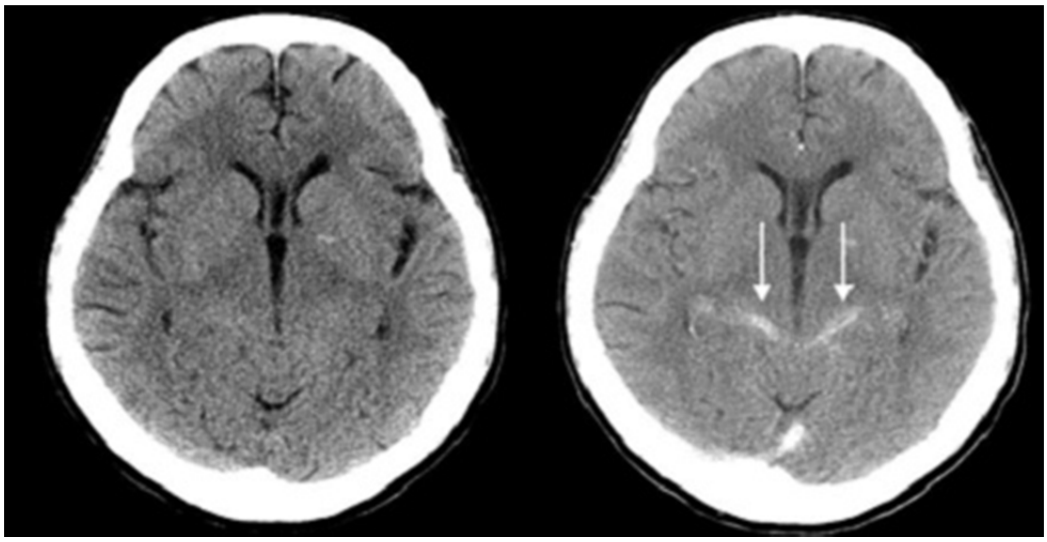


Figure 3.4 Cryptococcal meningitis presented leptomeningeal enhancement at bilateral basal cisterns (arrows) (12).

3.8.5 Tuberculous meningitis (TBM)

CT is seen as leptomeningeal thickening and enhancement predominantly involving the basal cisterns. Communicating hydrocephalus is a common sequel and is due to associated convexity involvement.

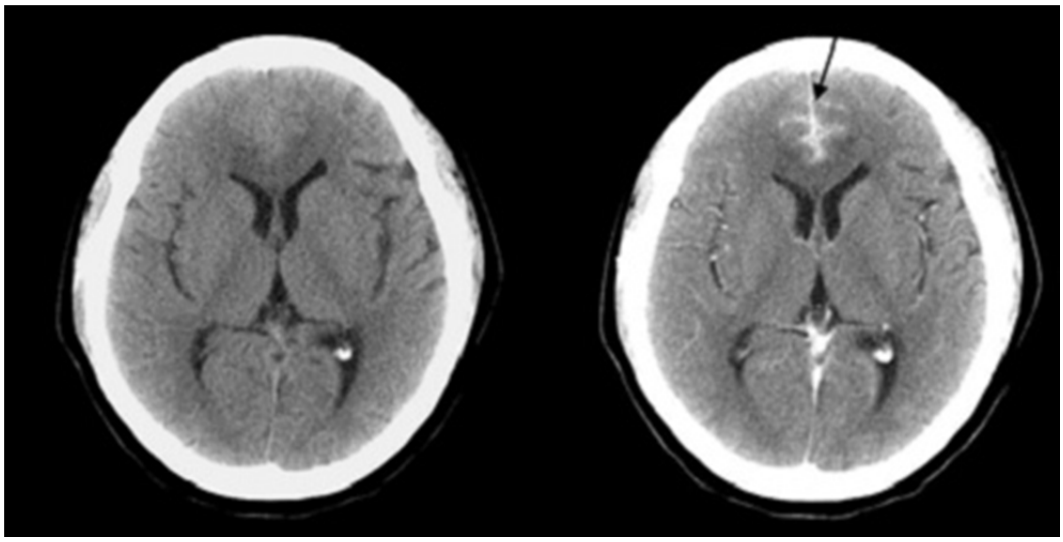


Figure 3.5 Tuberculous meningitis (TBM) presented leptomeningeal enhancement at subarachnoid space of the frontal lobe (arrow) (12).

3.8.6 Tuberculomas

CT shows ring enhancements single or multiple that sizes about 2-3 mm diameter and can develop to larger lesion. They may be hypodensity with rim enhancement, calcify (20%) on CT. However, they may be intracranial mass effect and edema, which led to show a symptom.

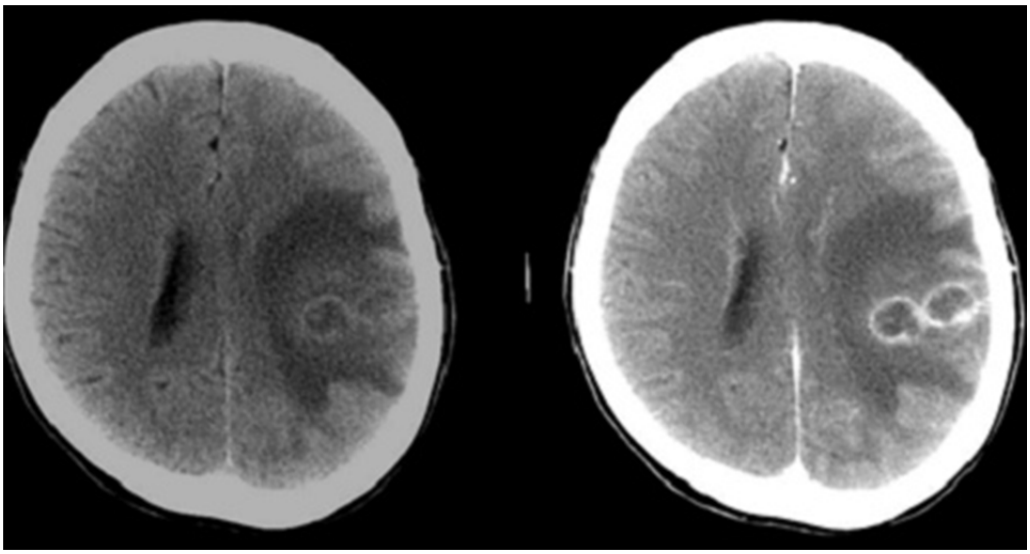


Figure 3.6 Tuberculomas presented rim-enhancing with central hyperdense lesions and perilesion edema at the left parietal lobe (12).

3.8.7 Toxoplasmosis

CT brain scan is usually shows ring-enhancement and single or multiple nodular low density areas in the gray matter of cortex or basal ganglia. Homogeneous enhancement is seen in small lesions and peripheral enhancements are usually seen in large lesions. Non-enhancement of lesion is uncommon. They are measured of size 1-4 cm. There is often with associated perilesional edema. The mimic lesion between Toxoplasmosis and other opportunistic include TB, these are less common but primary CNS lymphoma is the most difficult differential diagnosis from Toxoplasmosis. Therefore, MRI, SPECT and PET may be helpful in distinguishing.

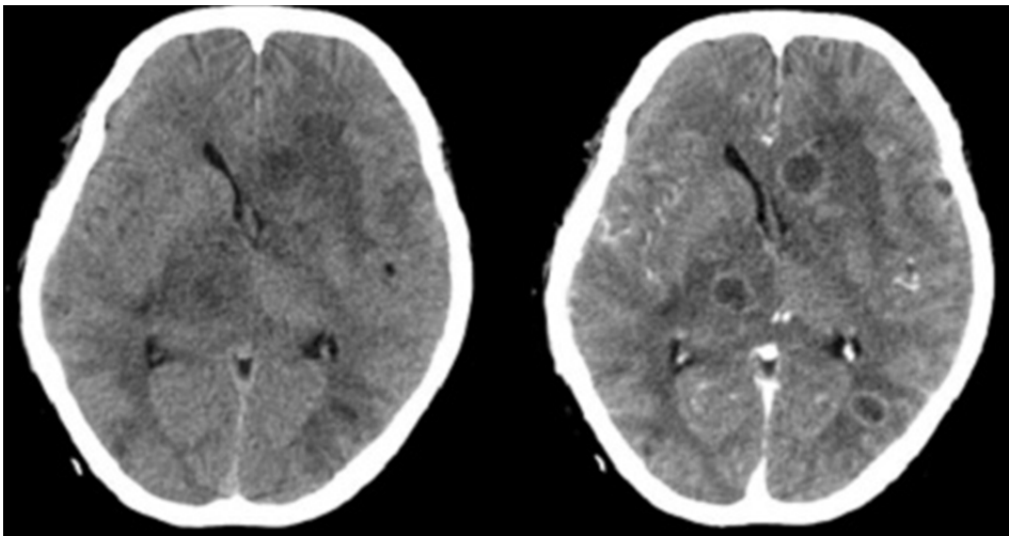


Figure 3.7 Toxoplasmosis presented multiple rim-enhancing lesions with perilesional edema at the left basal ganglion, right thalamus, left frontal and occipital lobes (12).

3.8.8 Primary CNS Lymphoma (PCNSL)

CT shows a solitary hyperdense mass. Multifocal lesions are seen in 50% of case. In 2006, Jitladda Ananwattanasuk and et al presented "Imaging Finding of CNS Lymphoma in Siriraj hospital". The most characteristic of pre-contrast was 45% of hyperdensity, followed by 33% of isodensity and 22% of hypodensity. The most characteristic of post-contrast was 78% of homogenous enhancement, followed by 11% of inhomogenous enhancement and 11% of ring enhancement that was all HIV-patients. Furthermore, leptominigeal enhancement could find 42%.

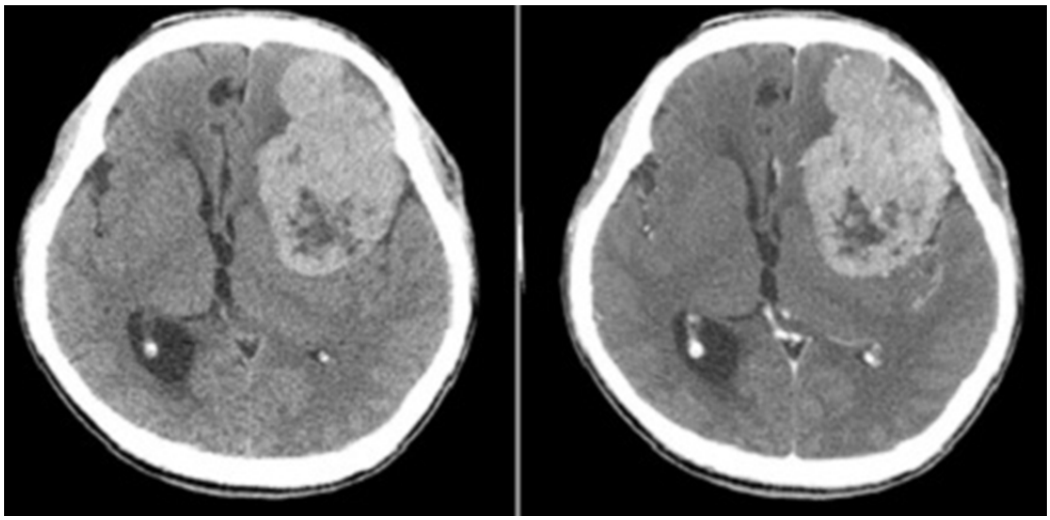


Figure 3.8 PCNSL presented homogeneous enhancing intra and extra-axial hyperdense mass with internal hypodense lesions and mass effect (12).

CHAPTER IV
MATERIALS AND METHODS

4.1 Materials

The patients were identified from The International Classification of Disease (ICD 10). The study was retrospective study by all patients that were available in assessment of both CT imaging of the brain in PACS workstation in Siriraj hospital and reviewed by two neuroradiologists. Our study corrected CT brain images of 139 HIV patients in Siriraj hospital since 2008 to 2013. Using the image data of CT brain in pre-contrast and post-contrast for diagnosis common neurological disease in HIV-patients have seropositive of HIV and with the mean age of 38.6±11.3 years (range 10-71 years). Accuracy of the study was done by using data of both CT imaging and medical record.

The CT scan was performed with multidetector CT scanner (Light speed 16; General Electric Medical System, Milwaukee, Wisconsin, USA). Technique: 120 kV, 250 mA, and 5-mm section thickness. Coverage was from the skull base to the vertex by obtaining contiguous axial.

4.2 Method

1. Baseline characteristic of the present were summarized in terms of frequency and percentages.

2. Agreements between interpretations of two neuroradiologists were calculated with the Cohen ‘kappa test.

Poor agreement = Less than 0.20

Fair agreement = 0.20 to 0.40

Moderate agreement = 0.41 to 0.60

Good agreement = 0.61 to 0.80

Very good agreement = 0.81 to 0.9

3. The result was analyzed from table 2*2 by using Microsoft Excel (Microsoft, 2010) and SPSS version 18. The accuracy of CT was calculated for sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV).

4.2.1 Calculation of sample size

The study of Ramathibodi hospital (12), which found 195 HIV patient associated with common neurological disease including HIV encephalitic (HIVE) 59 %, followed by Toxoplasmosis 22%, Cryptococcomas 9%, Tuberculous meningitis 5%, Tuberculomas 4%, Progressive multifocal leukoencephalopathy (PML) 3%, Lymphoma 2 %, and normal 1 %, Meningitis pattern 33%, Infarction 5% and Cerebritis 4 %. HIVE and Toxoplasmosis have high prevalence, therefore they are used to calculate the sample size of this study.

For HIV encephalopatchy with 97% sensitivity

As $N = Z_{\alpha/2^2}\, p(1-p) / d^2$

p = expected sensitivity 0.97

d = allowable error = 0.03

1-α = Confidence level = 0.95

α = 0.05(2-sided), $Z_{0.025}$ = 1.96

$$N = \frac{1.96^2(0.97)(0.03)}{0.03^2} = 124$$

And Toxoplasmosis with 90% sensitivity

$N = Z_{\alpha/2^2}\, p(1-p) / d^2$

p = expected sensitivity 0.9

d = allowable error = 0.1

1-α = Confidence level = 0.95

α = 0.05(2-sided), $Z_{0.025}$ = 1.96

$$N = \frac{1.96^2(0.1)(0.9)}{0.1^2} = 35$$

Therefore, the sample sizes of study are 35+124 = 159 patients.

4.2.2 Interpretation

The imaging interpretation were done by two neuroradiologists. Interestingly, some lesions from CT scan cannot classify the neurological disease. Accordingly, each diseases were reviewed for the following findings:

1. HIVE represented normal or atrophy, hypodense and no mass effect and non-enhancing**.**
2. Toxoplasmosis represented multiple hypodense/isodense lesions with surrounding edema and mass effect and thin, smooth rim or solid nodular enhancement surrounding edema and mass effect.
3. PML represented multifocal, hypodense without mass effect or edema and non-enhancing.
4. PCNSL represented isodense, hyperdense or hypodense ring-shaped, irregular and sometimes homogenous or rim enhancement.
5. TB meningitis represented isodense to hyperdense and leptominingeal enhacement.
6. Tuberculomas represented ring/nodular enhancing masses and edema and mass effect.
7. Cryptococcal meningitis represented isodense to hyperdense and leptominingeal enhacement.
8. Cryptococcomas represented a solid or ring enhancement parenchymal mass with surrounding edema and hydrocephalus.

CHAPTER V
RESULTS

5.1 Baseline patient characteristics

One hundred fifty nine patients had seropositive for HIV but twenty of all HIV patients were excluded for absent or poor data. Therefore, the study had all total 139 patients whose clinical and laboratory results had proven their HIV status as positive. All 139 patients presented clinical manifestations and underwent CT at Siriraj hospital from 2008 to 2013. The study of population included 93 males and 46 females with male-to-female ratio of 2:1 **(Table 5.1)**. The age of the patients ranged from 10 to 71 years with the mean age of 38.6±11.3 years. The three most of the patients were adult (range 21 to 60 years) including twenty-five patients (18%) were aged 21 to 30 years, seventy-six patients (54.7%) were aged 31 to 45 years and twenty-nine patients (20.9%) were aged 46 to 60 years **(Table 5.1)**.

Table 5.1 characteristic of 139 HIV-patients

Patient characteristic	**Number (%)**
Sex	
Male	93 (67.0)
Female	46 (33.1)
Age group	
>20	4 (2.9)
21-30	25 (18.0)
31-45	76 (55.0)
46-60	29 (20.9)
>60	5 (3.6)

5.2 Laboratory investigation

5.2.1 HIV infectionhhhhhhhh

Most of the T-helper or CD4-counts were less than 200 cells/mm^3 (128 patients, 92.1%). Ten patients (7.2%) were 200-500 cells/mm^3. One patient (0.7%) was greater than 500 cells/mm^3. The median CD4-counts were 50 cells/ mm^3 (range 1-656 cells/ mm^3) **(Table 5.2)**. Most of the white blood cells were 3,000-10,000 cells/mm^3 (107 patients, 77%). Eight teen patients (13%) were greater than 10,000 cells/mm^3. Fourteen patients (10.1%) were less than 3,000 cells/mm^3. The median white blood cells was 5,630 cells/mm^3 (range 960-183,000 cell/ mm^3)**(Table 5.2)**.

Table 5.2 CD4-count and White blood cell of 139 HIV-patients

Patient characteristic	**Number (%)**
CD 4 count (cells/mm^3)	
<200	128 (92.1)
200-500	10 (7.2)
>500	1 (0.7)
White blood cell (cell/mm3)	
<3000	14 (10.1)
3,000-10,000	107 (77.0)
>10,000	18 (13.0)

Note: normal CD4 = 500-1,500 cell/mm^3 and normal white blood cell = 3,000-10,000 cell/mm^3

5.2.2 HIV associated common neurological diseases

All 139 HIV patients associated common neurological diseases. Most common neurological disease was Cryptococcal meningitis (46 patients, 33.1%), followed by Tuberculous meningitis (45 patients, 32.4%), HIVE (37 patients, 26.6%), Toxoplasmosis (20 patients, 14.4%), PML (13 patients, 9.4%), PCNSL (9 patients, 6.5%), Other (Brain metastasis, Intracerebral hemorrhage, Meningitis and Kaposi sarcoma) (5 patients, 3.6%), Tuberculomas (4 patients, 2.9%), and Cryptococcomas (3 patients, 2.2%). Most of the patients had more than one disease **(Table 5.3)**.

Table 5.3 Prevalence of common neurological diseases of 139 HIV-patients from 2008 to 2013 at Siriraj hospital.

Common neurological diseases	**Number (%)**
Cryptococcal meningitis	46 (33.1)
Tuberculous meningitis	45 (32.4)
HIVE	37 (26.6)
Toxoplasmosis	20 (14.4)
PML	13 (9.4)
PCNSL	9 (6.5)
Other	5 (3.6)
Tuberculomas	4 (2.9)
Cryptococcomas	3 (2.2)

All 46 of 139 patients that were confirmed by laboratory test for Cryptococcal meningitis. All 34 of 46 patients were received cerebrospinal fluid antigen (CSF-antigen), the negative result was 2 patients and the positive result was 32 patients. All 5 of 46 patients were received cerebrospinal fluid polymerase chain reaction (CSF-PCR), the negative result was 3 patients and the positive result was 2 patients. All 42 of 46 were received India ink, the negative result was 9 patients and the positive result was 33 patients. All 5 of 46 were received Toxoplasmosis Ag, the negative result was 3 patients and the positive result was 2 patients **(Table 5.4)**.

All 45 of 139 patients that were confirmed by laboratory test for Tuberculous meningitis. All 39 of 45 patients were received cerebrospinal fluid antigen (CSF-antigen), the negative result was 33 patients and the positive result was 6 patients. All 15 of 45 patients were received cerebrospinal fluid polymerase chain reaction (CSF-PCR), the negative result was 7 patients and the positive result was 8 patients. All 35 of 45 were received India ink, the negative result was 33 patients and

the positive result was 2 patients. All 9 of 45 were received Toxoplasmosis Ag, the negative result was 7 patients and the positive result was 2 patients **(Table 5.4)**.

All 37 of 139 patients that were confirmed by laboratory test for HIVE. All 26 of 37 patients were received cerebrospinal fluid antigen (CSF-antigen), the negative result was 15 patients and the positive result was 11 patients. All 20 of 37 patients were received cerebrospinal fluid polymerase chain reaction (CSF-PCR), the negative result was 17 patients and the positive result was 3 patients. All 27 of 37 were received India ink, the negative result was 17 patients and the positive result was 10 patients. All 17 of 37 were received Toxoplasmosis Ag, the negative result was 13 patients and the positive result was 4 patients **(Table 5.4)**.

All 20 of 139 patients that were confirmed by laboratory test for Toxoplasmosis. All 18 of 20 patients were received cerebrospinal fluid antigen (CSF-antigen), the negative result was 13 patients and the positive result was 5 patients. All 1 of 20 patients were received cerebrospinal fluid polymerase chain reaction (CSF-PCR), the positive result was 1 patient. All 15 of 20 were received India ink, the negative result was 9 patients and the positive result was 6 patients. All 17 of 20 were received Toxoplasmosis Ag, the negative result was 5 patients and the positive result was 12 patients **(Table 5.4)**.

All 13 of 139 patients that were confirmed by laboratory test for PML. All 9 of 13 patients were received cerebrospinal fluid antigen (CSF-antigen), the negative result was 8 patients and the positive result was 1 patient. All 2 of 13 patients were received cerebrospinal fluid polymerase chain reaction (CSF-PCR), the negative result was 2 patients. All 8 of 13 were received India ink, the negative result was 8 patients. All 3 of 13 were received Toxoplasmosis Ag., the negative result was 3 patients **(Table 5.4)**.

All 9 of 139 patients that were confirmed by laboratory test for PCNSL. All 3 of 9 patients were received cerebrospinal fluid antigen (CSF-antigen), the negative result was 2 patients and the positive result was 1 patient. All 4 of 9 were received India ink, the negative result was 4 patients. All 4 of 9 were received Toxoplasmosis Ag., the negative result was 3 patients and the positive result was 1 patient **(Table 5.4)**.

All 4 of 139 patients that were confirmed by laboratory test for Tuberculomas. All 3 of 4 patients were received cerebrospinal fluid antigen (CSF-antigen), the negative result was 3 patients. No any patient was received cerebrospinal fluid polymerase chain reaction (CSF-PCR). All 2 of 4 were received India ink, the negative result was 2 patients. All 2 of 4 were received Toxoplasmosis Ag, the negative result was 2 patients **(Table 5.4)**.

All 5 of 139 patients that were confirmed by laboratory test for other diseases. All 1 of 5 patients was received cerebrospinal fluid antigen (CSF-antigen), the negative result was 1 patient. Not any patient was received cerebrospinal fluid polymerase chain reaction (CSF-PCR). All 1 of 5 was received India ink, the negative result was 1 patient. Not any patient was received Toxoplasmosis Ag **(Table 5.4)**.

All 3 of 139 patients that were confirmed by laboratory test for Cryptococcomas. All 2 of 3 patients were received cerebrospinal fluid antigen (CSF-antigen), the positive result was 2 patients. Not any patient was received cerebrospinal fluid polymerase chain reaction (CSF-PCR). All 2 of 3 were received India ink, the positive result was 2 patients. All 2 of 3 patient was received Toxoplasmosis Ag, the negative result was 2 patients **(Table 5.4)**.

Finally, All 10 of 139 patients were diagnosed by biopsy including 4 patients, 3 patients, 1 patient, 1 patient and 1 patient of PCNSL, Tuberculomas, Toxoplasmosis, PML and Cryptococcomas respectively **(Table 5.4)**.

Table 5.4 Investigation for common neurological diseases of 139 HIV patients.

Neurological diseases	CSF-antigen		CSF-PCR		India ink		Toxoplasmosis Ag		Biopsy
	(-)	(+)	(-)	(+)	(-)	(+)	(-)	(+)	(+)
Cryptococcal meningitis	2	32	3	2	9	33	3	2	-
Tuberculous meningitis	33	6	7	8	33	2	7	2	-
HIVE	15	11	17	3	17	10	13	4	-
Toxoplasmosis	13	5	0	1	9	6	5	12	1
PML	8	1	2	-	8	-	3	-	1
PCNSL	2	1	-	-	4	-	3	1	4
Tuberculomas	3	-	-	-	2	-	2	-	3
Other	1	-	-	-	1	-	-	-	-
Cryptococcomas	-	2	-	-	-	2	2	-	1

5.3 Clinical manifestations

All 139 HIV patients associated common neurological diseases. Most common neurological symptom was headache (100 patients, 71.94%), followed by weakness (75 patients, 53.96%), nausea/vomiting (58 patients, 41.73%), altered consciousness (55 patients, 39.57%), blurred vision (37 patients, 26.62%), stiff neck (29 patients, 20.86%), seizures (27 patients, 19.42%), ataxia (20 patients, 14.39%), diplopia (10 patients, 7.19%) and numbness (2 patients,1.44%) **(Table 5.5)**.

Table 5.5 Neurological symptoms of 139 HIV-patients.

Neurological symptom	Number (%)
Headache	100 (72.0)
Weakness	75 (54.0)
Nausea/vomiting	58 (41.7)
Altered consciousness	55 (39.6)
Blurred vision	37 (26.6)
stiff neck	29 (20.9)
Seizures	27 (19.4)
Ataxia	20 (14.4)
Diplopia	10 (7.2)
Numbness	2 (1.4)

Most extra-neurological symptom was fever (102 patients, 73.4%), followed by cough (53 patients, 38.1%), weight loss (48 patients, 34.5%), skin rash (15 patients, 10.8%), diarrhea (8 patients, 5.8%), abdominal pain (6 patients, 4.3%), dyspnea (2 patients, 1.4%), chills (2 patients, 1.4%) and tremble (2 patients, 1.4%) **(Table 5.6)**.

Table 5.6 Extra-neurological symptoms of 139 HIV-patients.

Extra-neurological symptoms	Number (%)
Fever	102 (73.4)
Cough	53 (38.1)
Weight loss	48 (34.5)
Skin rash	15 (10.8)
Diarrhea	8 (5.7)
Abdominal pain	6 (4.3)
Dyspnea	2 (1.4)
Chills	2(1.4)
Tremble	2 (1.4)

5.4 Interpretation with computer tomography by calculated statistic

5.4.1 Interobserver agreement

The CT-finding was presented by two neuroradiologists. It was calculated with Kappa. Interpretation for Cryptococcal meningitis was good agreement (K=0.7), TB meningitis was good agreement (K=0.7), HIVE was moderate agreement (K=0.5), Toxoplasmosis was good agreement (K=0.7), PML was good agreement (K=0.8), PCNSL was very good agreement (K=0.9), Tuberculomas was moderate agreement (K=0.6), Other (Brain metastasis, Intracerebral hemorrhage, Meningitis and Kaposi sarcoma) were moderate agreement (K=0.5) and interpretation of Cryptococcomas was fair agreement (K=0.4) (**Table 5.7)**.

Table 5.7 Agreement between interpretations of two neuroradiologists for common neurological diseases (139 patients).

Common neurological disease	Neurological 1 and Neurological 2				
	A (+ +)	B (+ -)	C (- +)	D (- -)	Kappa
Cryptococcal meningitis	34	7	12	86	0.7
Tuberculous meningitis	21	10	2	106	0.7
HIVE	63	3	26	47	0.6
Toxoplasmosis	26	9	7	97	0.7
PML	18	4	1	116	0.8
PCNSL	8	1	0	130	0.9
Tuberculomas	5	1	5	128	0.6
Other	9	6	9	115	0.5
Cryptococcomas	2	0	6	131	0.4

5.4.2 Calculated statistic for accuracy of computer tomography

Cryptococcal meningitis was diagnosed in 34 patients by CT and 46 patients in medical record. There were 18 patients of true positive and false negative in 28 patients including 17 HIVE, 4 TB meningitis, 3 PML combined with HIVE, 1 PML, 1 Toxoplasmosis, 1 Tuberculomas and 1 Toxoplasmosis combined Tuberculomas. The Specificity, Sensitivity, PPV, NPV and Accuracy of Cryptococcal meningitis was 82.8%, 39.1%, 52.9%, 73.3% and 68.3% respectively **(Table 5.8)**. TB meningitis was diagnosed 21 patients by CT and 45 patients medical record. There were 15 patients of true positive and 30 patients of false negative including 10 HIVE, 8 Cryptococcal meningitis, 5 HIVE combined with Cryptococcal meningitis, 2 Toxoplasmosis, 2 Other (Meningitis pattern), 1 Toxoplasmosis combined with Cryptococcomas and Cryptococcal meningitis, 1 Tuberculomas and 1 PML. Seven patients of false positive were 6 Cryptococcal meningitis. The Specificity, Sensitivity, PPV, NPV and Accuracy of TB meningitis was 93.6%, 33.3%, 71.4%, 74.6% and 74.1% respectively **(Table 5.8)**. HIVE was diagnosed in 63 patients by CT and 37 patients in medical record. There were 20 patients of true positive and false negative in 17 patients including 7 Toxoplasmosis, 3 other (Meningitis pattern), 3 TB meningitis,

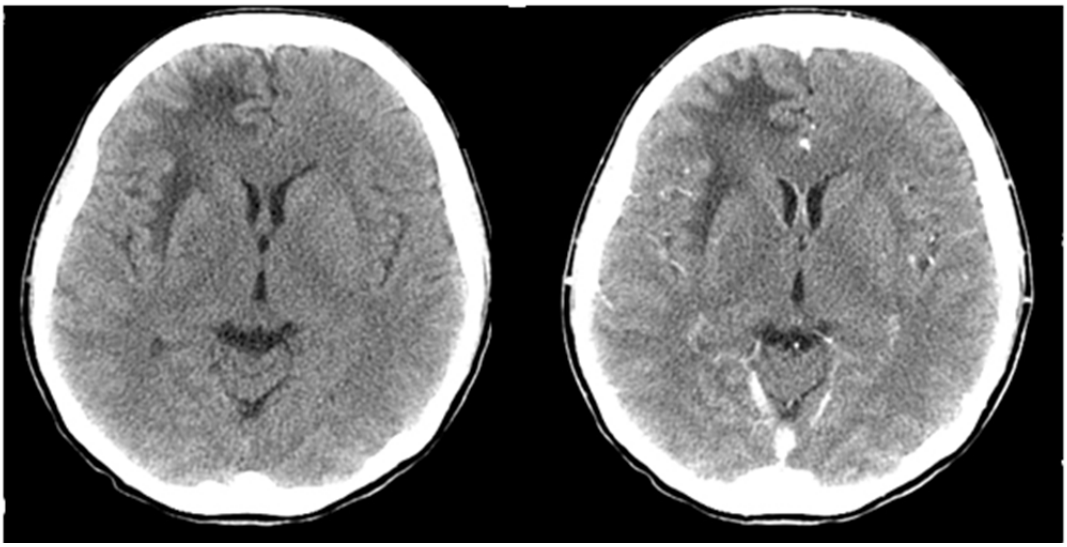
2 Cryptococcal meningitis, 1 PML and 1 Tuberculomas. The Specificity, Sensitivity, PPV, NPV and Accuracy of HIVE were 57.8%, 54.1%, 31.7%, 77.6% and 56.8% respectively **(Table 5.8)**. Toxoplasmosis was diagnosed 26 patients by CT and 20 patients in medical record. There were 16 patients of true positive and 4 patients of false negative including 1 HIVE, 1 PML, 1 HIVE combined with PML and 1 HIVE combined with Cryptococcal meningitis. The Specificity, Sensitivity, PPV, NPV and Accuracy of Toxoplasmosis was 91.6%, 80.0%, 61.5%, 96.5% and 89.9 % respectively **(Table 5.8)**. PML was diagnosed 18 patients by CT and 13 patients in medical record. There were 11 patients of true positive and 2 patients of false negative including 2 HIVE. The Specificity, Sensitivity, PPV, NPV and Accuracy of PML were 94.4%, 84.6%, 61.1%, 98.3% and 93.5% respectively **(Table 5.8)**. PCNSL was diagnosed 8 patients by CT and 9 patients in medical record. There were 7 patients of true positive and 2 patients of false negative including 2 Toxoplasmosis. The Specificity, Sensitivity, PPV, NPV and Accuracy of PCNSL was 99.2%, 77.8%, 87.5%, 98.5% and 97.8% respectively **(Table 5.8)**. Tuberculomas was diagnosed 5 patients by CT and 4 patients in medical record. There were 2 patients of true positive and 2 patients of false negative including 2 Toxoplasmosis. Three patients of false positive were 2 Cryptococcal meningitis and 1 TB meningitis. The Specificity, Sensitivity, PPV, NPV and Accuracy of Tuberculomas was 97.8%, 50.0%, 40%, 98.5% and 96.4% respectively **(Table 5.8)**. The others were diagnosed 9 patients by CT and 5 patients in medical record. There were 2 patients of true positive and 3 patients of false negative. The Specificity, Sensitivity, PPV, NPV and Accuracy of the others was 95.8.1%, 40.0%, 22.2.0%, 97.8% and 92.8.0% respectively **(Table 5.8)**. Cryptococcomas was diagnosed 2 patients by CT and 2 patients in medical record. There was 0 patient of true positive and 2 patients of false negative including 2 Tuberculomas. The Specificity, Sensitivity, PPV, NPV and Accuracy of Cryptococcomas was 98.5%, 0%, 0%, 97.8% and 96.4% respectively **(Table 5.8)**.

Table 5.8 PPV, NPV, Sensitivity, Specificity and Accuracy of Computed tomography for interpretation in 139 HIV patients TP = True positive TN = True negative FN=False negative FP=False positive PPV=Positive predictive positive value NPV=Negative predictive value

Common neurological disease	CT/ final diagnosis				CT pattern				
	TP (no.)	TN (no.)	FP (no.)	FN (no.)	PPV (95% CI)	NPV (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Accuracy
Cryptococcal meningitis	18	77	16	28	52.9(35.4-69.8)	73.3(63.6-81.3)	39.1(25.4-54.6)	82.8(73.2-89.5)	68.3
TB meningitis	15	88	6	30	71.4(47.7-87.8)	74.6(65.6-81.9)	33.3(20.4-49.1)	93.6(86.1-97.4)	74.1
HIVE	20	59	43	17	31.7(20.9-44.8)	77.6(66.3-86.1)	54.1(37.1-70.2)	57.8(47.7-67.4)	56.8
oxoplasmosis	16	109	10	4	61.5(40.7-79.1)	96.5(90.6-98.9)	80.0(55.7-93.4)	91.6(84.7-95.7)	89.9
PML	11	119	7	2	61.1(36.1-81.7)	98.3(93.6-99.7)	84.6(53.7-97.3)	94.4(88.5-97.5)	93.5
PCNSL	7	129	1	2	87.5(56.0-98)	98.5(95.0-99.6)	77.8(45.3-93.7)	99.2(95.8-99.9)	97.8
Tuberculomas	2	132	3	2	40.0(7.2-82.9)	98.5(94.2-99.7)	50.0(9.1-90.8)	97.8(93.1-99.4)	96.4
Other	2	127	7	3	22.2(3.9-59.8)	97.7(92.9-99.4)	40.0(7.2-82.9)	94.8(89.1-97.7)	92.8
Cryptococcomas	0	134	2	3	0.0(0.0-80.2)	97.8(93.2-99.4)	0.0(0.0-69.0)	98.5(94.2-99.7)	96.4

5.5 CT-finding of HIV associated common neurological diseases

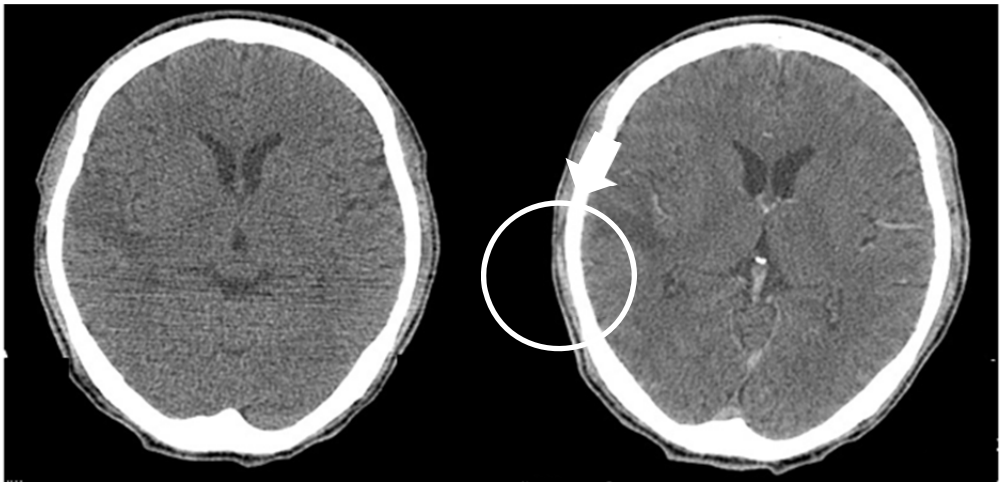
5.5.1 Progressive multifocal leukoencephalopathy (PML)



Pre contrast **Post contrast**

Figure 5.1 A 44 years old-female with CD4 count 179 cells/mm^3. CT finding shows hypodensity at Rt.frontal white matter. CSF-antigen for JC virus was positive result.

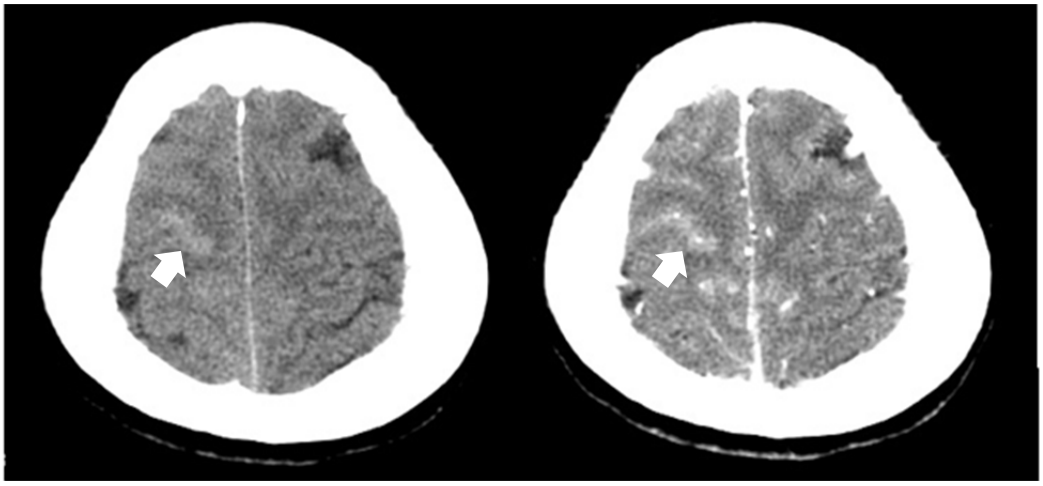
5.5.2 Tuberculous meningitis



Pre contrast **Post contrast**

Figure 5.2 A 43 years old-male. CT finding shows hypodense non-enhancement (arrow) at Rt.temporal lobe infarction. Final diagnosis was proved by toxoplasma IgG which had negative result and CSF-antigen for cryptococcoal was negative result

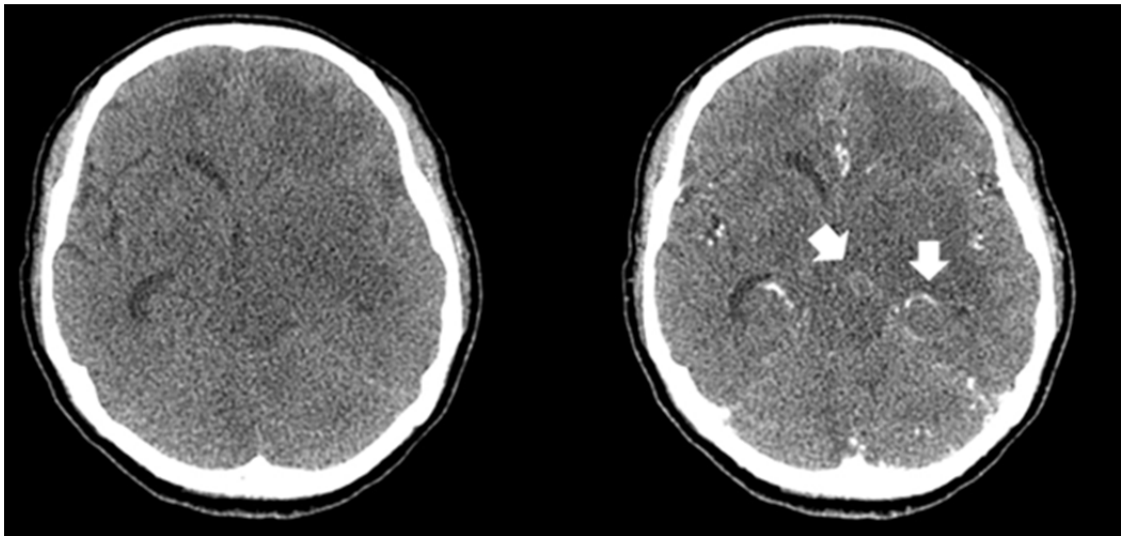
5.5.3 Cryptococcal meningitis



Pre contrast **Post contrast**

Figure 5.3 A 55 years old-female. CT finding shows hyperdense leptomeningeal enhancement (arrow) at Rt.Frontal lobe and brain swelling and cortical atrophy. Final diagnosis was proved by CSF-antigen for cryptococcoal which had positive result.

5.5.4 Toxoplasmosis

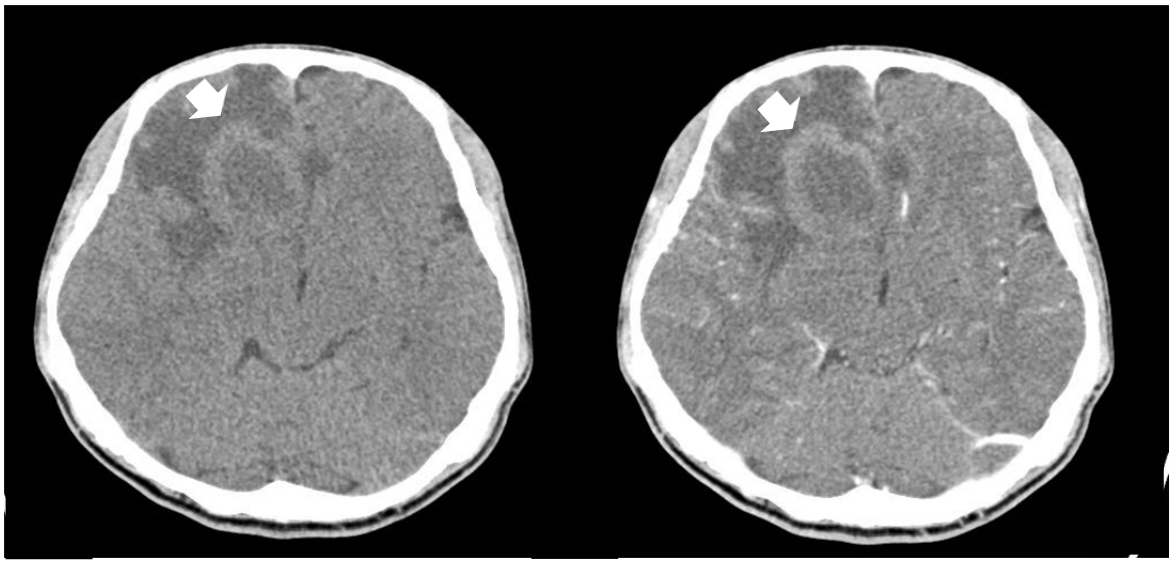


Pre contrast **Post contrast**

Figure 5.4 A 33 years old-female with CD4 count 148 cells/mm^3. She has history of fever and progressive deterioration of consciousness. CT finding shows the study reveals diffuse multifocal areas of hypodensity involving corticomedullary junction, deep gray and white matter of Lt. cerebral hemisphere, both sides of brain stem and cerebellum. Effectment of sulci and gyri of Lt. cerebral hemisphere is demonstrated. These findings are compatible with vasogenic brain edema. Partial obliteration of frontal and temporal horn of Lt. lateral ventricle is also noted.

Post contrast: There are rather ill-defined abnormal nodular rim enhancing lesions with perilesional edema at Lt. basal ganglia and midbrain, measured about 0.8x0.8 cm. and 0.9x0.9 cm respectively. Final diagnosis was proved by toxoplasma IgG which had positive result.

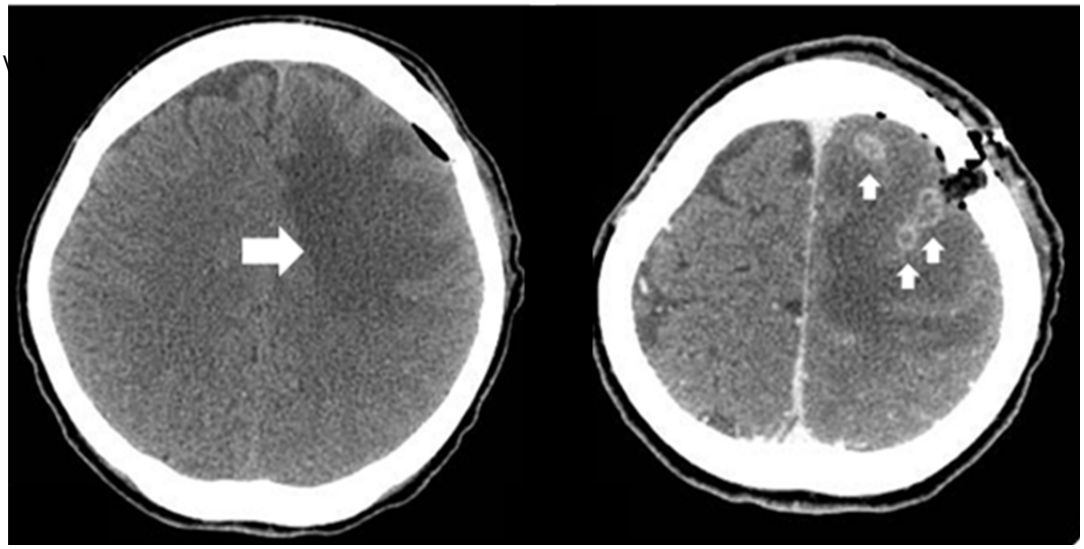
5.5.5 Primary CNS lymphoma



Pre contrast **Post contrast**

Figure 5.5 A 31 years old-male with CD4 count 50 cells/mm^3. CT shows ring enhancement lesion at Rt. frontal lobe with mass effect, another ring enhancing lesion at Rt. Parietal lobe. Final diagnosis was proved by toxoplasma IgG which had negative result. The case of corrected diagnosed PCNSL by CT.

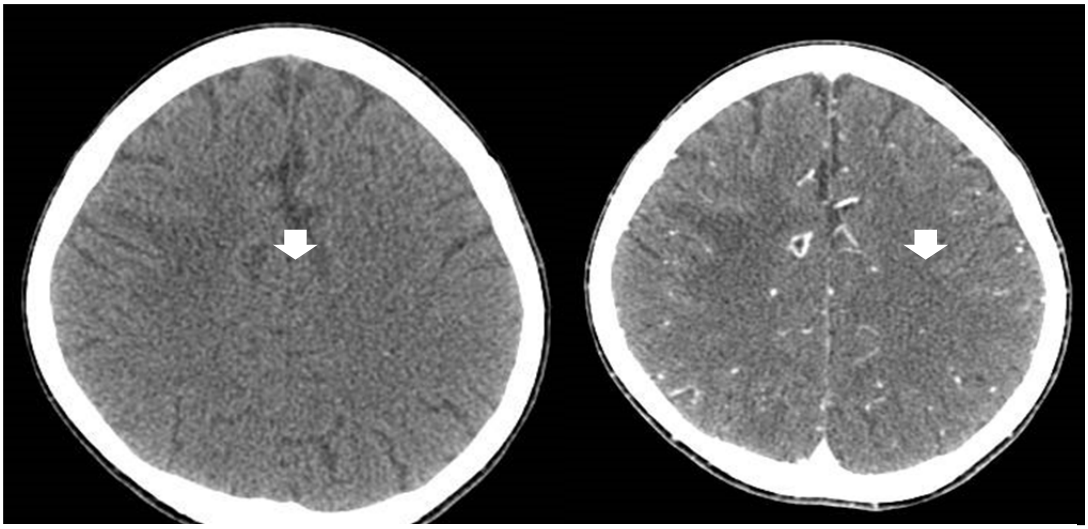
5.5.6 Tuberculomas



Pre contrast **Post contrast**

Figure 5.6 A 32 years old-male with CD4 count 130 cells/mm^3. CT finding shows hypodensity lesion at Lt.frontal lobe with perilesional vasogenic edema and ring enhancement lesion at gray white junction. CT diagnosed Toxoplasmosis. Final diagnosis was proved by toxoplasma IgG which had negative result. Biopsy was proved in Tuberculoma

5.5.7 Cryptococcomas



Pre contrast **Post contrast**

Figure 5.7 A 39 years old-female with CD4 count 54 cells/mm^3. CT finding shows low density lesion with ring enhancement at right fronto-parietal area with peri-lesional edema. The case of uncorrected diagnosed Toxopalsmosis by CT. Final diagnosis was proved by CSF of cryptococosis antigen which had positive result and toxoplasma IgG negative result.

CHAPTER VI
DISCUSSION

HIV associated common neurological diseases are an important disease for health problem and may lead the high mortality. Up to 60% of all HIV patients will be developed common neurological diseases (23). HIV patient can be appearance of various diseases and often are diagnosed with imaging in order to find out a real cause. Therefore, Computer tomography (CT) is a choice of diagnosis.

The present study shows male to female with ratio of 2:1 and the mean age of 38.6±11.3 years. Most CD4 count was less than 200 cells/mm^3 (128 patients, 92.9%) with the median CD4 count of 50 cells/ mm^3(range 1- 656 cells/ mm^3). However, HIV patients with less than 200 cells/mm^3 will be developed certain opportunistic infection (24). Therefore, this range is found about 50-70% and is the highest risk in the patients. If they did not receive antiretroviral therapy, they would have CD4 count of less than 50 cells/mm^3 and show of common neurological diseases within 2 years (25).

The prevalence of the present study in 139 HIV patients associated common neurological diseases of Cryptococcal meningitis (46 patients, 32.6%), TB meningitis (45 patients, 32.4%), HIVE (37 patients, 26.6%), Toxoplasmosis (20 patients, 14.4%), PML (13 patients, 9.4%), PCNSL (9 patients, 6.5%), Other (Brain metastasis, Intracerebral hemorrhage, Meningitis and Kaposi sarcoma) (5 patients, 3.6%), Tuberculomas (4 patients, 2.9%), and Cryptococcomas (3 patients, 2.2%) in period 2008 to 2013 at Siriraj hospital. There were many author about HIV patients associated common neurological diseases such as, the study of Masliah E et al, who reviewed brain 390 AID patients in period 1982 to 1998.The result showed HIVE 26.3%, CMV 22.3%, Toxoplasmosis 2.51%, PML 2.9% and non-hodgkins'lymphoma 8.4%. The study of Steinmetz H et al reviewed brain 188 HIV patients in period 1988 to 1991. The result showed cerebral Toxoplasmosis 25%, HIVE 10.1%, PML 4.8%, cerebral Lymphoma 0.5% and other conditions 4.8%. From, the report of Thailand, a

retrospective study of Ramathibodi hospital reviewed 195 HIV patients in period 2001-2005.The result showed HIVE 59%, Toxoplasmosis 22%, Cryptococcomas 9%, Tuberculous meningitis 5%, Tuberculomas 4%, PML 3%, Lymphoma 2% and normal 1%. And the retrospective study of King Chulalongkorn Memorial Hospital reviewed 148 HIV-patients in period 2007-2008. The result showed Cryptococcal meningitis (56 patients, 37.8%), followed by tuberculosis (53patients, 35.8%), toxoplasmosis(19 patients, 12.8%), progressive multifocal leukoencephalopathy (6patients, 4.1%), varicella-zoster virus (VZV) meningitis (4patients, 2.7%), brainabscess (3patients, 2.1%), cytomegalovirus radiculomyelitis (2patients, 1.4%), pneumococcal meningitis (2patients, 1.4%), herpes simplex encephalitis, Epstein-Barr virus-related primary CNS lymphoma, and HIV-associated myelopathy (1 patient, 1 patient, 0.7%).However, those reports found difference of common neurological diseases in each report causing from the prevalence of HIV patients in difference area and period of collecting data.

Cryptococcal meningitis is the most common neurological disease from opportunistic infection causing meningitis pattern. In the report **(16)**, Cryptococcus infection is the third most common cause of CNS infection in AIDS patients. A characteristic pattern shows isodense to hyperdense and Leptominingeal enhacement **(Figure 5.3)** being also seen meningitis involvement. However, CT could not identify real cause of meningitis form. However, Cryptococcal meningitis, there were 17 cases of HIVE and 4 cases of TB meningitis being false negative. As, the Specificity, Sensitivity, PPV and NPV was 82.8%, 39.1%, 52.9% and 73.3% respectively **(Table 5.8)**. For Cryptococcomas shows a solid or ring enhancement parenchymal mass with surrounding edema and hydrocephalus **(Figure 5.7)**. There were 2 cases of Tuberculomas being false negative. The Specificity, Sensitivity, PPV and NPV of the others was 98.5%, 0%, 0% and 97.8% respectively **(Table 5.8)**. For, TB meningitis can occur in 5-10% of TB patients with HIV infection which are compared with 2-5% of TB patients without HIV infection (18). The TB shows isodense to hyperdense and Leptominingeal enhacement **(Figure 5.2)**, which seems Cryptococcal meningitis. The study had 10 cases of HIVE and 8 Cryptococcal meningitis being false negative. The Specificity, Sensitivity, PPV and NPV was 93.6%, 33.3%, 71.4% and 74.6% respectively **(Table 5.8)**. However, Tuberculomas shows ring/nodular enhancing with

surrounding edema and mass effect **(Figure 5.6)**. Furthermore, when CT shows ring enhancement pattern, it could not be difficult to identify in brain abscess. The present had 2 cases of Toxoplasmosis being false negative. In the study had associated finding with ring enhancement confirmed by brain biopsy. There was Specificity, Sensitivity, PPV and NPV of Tuberculomas (97.8%, 50.0%, 40% and 98.5% respectively)**(Table 5.8)**. For PML is cause from the papova virus. The incidence of PML with AIDS patients is about 3%-7% of all patients and can be found in childrenhood and adults. The PML shows hypodense lesions of the white matter with no mass effect and non-enhancement **(Figure 5.1)**. There was Specificity, Sensitivity, PPV and NPV (94.4%, 84.6%, 61.1% and 98.3% respectively). And there were 2 cases of HIVE being false negative by CT **(Table 5.8).** However, CT could be used for both diagnosis and exclusion of the disease. The Toxoplasmosis is the most common cause of focal brain lesions in 3-40% of patients. A characteristic shows single lesion or multiple lesions with surrounding edema, with contrast shows ring enhancement and size < 4 cm. **(Figure 5.4)**.There was Specificity, Sensitivity, PPV and NPV (91.6%, 80.0%, 61.5% and 96.5% respectively) **(Table 5.8)**. The incidence of AIDS patient with PCNSL is about 5%. It can appear both HIV patients and non-HIV patients but the risk of HIV patients was more than in non-HIV patients. CT finding shows single or multiple hypodense lesions, with contrast shows homogenous, ring enhancing and mass effect with size > 4 cm and surrounding edema **(Fig 5.6)**. There was high Specificity, Sensitivity, high PPV and NPV of PCNSL (99.2%, 77.8%, 87.5% and 98.5% respectively). However, CT may be difficult to identify between Toxoplasmosis and PCNSL. The present, there were 2 cases of Toxoplasmosis being false negative. In the study had associated finding with ring enhancement confirmed by brain biopsy **(Table 5.8)**. Finally, HIVE is the primary infection of CNS causing of AIDS-dementia or subcortical dementia. HIVE occur later stages of HIV infection. The incidence of HIVE is about 10-30% of AIDS patients. On image shows normal or atrophy (usually can find in adult patient with age more than 60 years), hypodense and no mass effect and non-enhancing and may be overlap with other the diseases. In the present, there was Specificity, Sensitivity, PPV and NPV for HIVE (57.8%, 54.1%, 31.7% and 77.6% respectively) **(Table 5.8).**

Moreover, the present study for accuracy of cranial computer tomography for Cryptococcal meningitis, TB meningitis, HIVE, Toxoplasmosis, PML, PCNSL, Tuberculomas, Other (Brain metastasis, Intracerebral hemorrhage, 2 Meningitis and Kaposi sarcoma) and Cryptococcomas was 68.3, 74.1, 56.8, 89.0, 93.5, 97.8, 96.4, 92.8 and 96.4 respectively. The most accuracy of CT was focal neurological diseases such as PCNSL (97.8%), PML (93.5%), Tuberculomas (96.4%) and Cryptococcomas (96.4%) and Toxoplasmosis (89.0%) followed by HIVE (56.8%) and Meningitis pattern.

Therefore, the regulation of this study is Brain abscess shows ring enhancement which it may be confused between Toxoplasmosis, Tuberculomas and Cryptococcomas. They will confirmed by laboratory test such as, brain biopsy. For meningitis pattern cannot identify cause of each disease in some patients. It has just showed with leptomeningeal enhancement for helpful to diagnosis meningitis pattern. Moreover, some of the patients have combine with HIVE resulting do not separate opportunistic infection and HIVE as CT cannot identify cause of the disease. However, it can useful for primary diagnosis.

CHAPTER VII
CONCLUSION

In this study is education of Siriraj hospital from 2008 to 2013 finding all 159 HIV patients associated common neurological diseases had seropositive for HIV but 20 patients of all HIV patients were excluded for absent or poor data. As, the study had all 139 patients whose clinical and laboratory results had proven their HIV status as positive. All 139 patients presented clinical manifestations and underwent CT at Siriraj hospital. However, some patients are overlap of various diseases. Therefore, computer tomography (CT) can find cause of each disease.

As the result, most accuracy was PCNSL (97.8%), followed by, Tuberculomas (96.4%), Cryptococcomas (96.4%), PML (93.5%), Toxoplasmosis (89.9%), TB meningitis (74.1%), Cryptococcal meningitis (68.3%) and HIVE (56.8%). The most of prevalence was Cryptococcal meningitis (46 patients, 33.1%), followed by TB meningitis (45 patients, 32.4%), HIVE (37 patients, 26.6%), Toxoplasmosis (20 patients, 14.4%), PML (13 patients, 9.4%), PCNSL (9 patients, 6.5%), Other (Brain metastasis, Intracerebral hemorrhage, Meningitis and Kaposi sarcoma) (5 patients, 3.6%), Tuberculomas (4 patients, 2.9%), and Cryptococcomas (3 patients, 2.2%) However, if they are treated with Highly Active Antiretroviral Therapy (HAART), they will have decrease mortality. Therefore, this study has just found the correct diagnosis of each disease in order to lead more efficiency of treatment.

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APPENDICES

APPENDIX A

1. Calculation by Excel 2010

This study use statistic such as mean and median which obtained from the information of population in each samples

a. Mean standard deviation (Mean ± SD)

Mean is the average and is computed as the sum of all the observed outcomes from the sample divided by the total number of events. We use x as the symbol for the sample mean.

Mean =AVERAGE (number 1, [number 2], …)

Standard deviation is A measure of the dispersion of a set of data from its mean. The more spread apart the data, the higher the deviation. Standard deviation is calculated as the square root of variance.

SD =STDEV (number 1, [number 2], …)

b. Median

Median is the middle value of the data set when it has been arranged in ascending order. That is, from the smallest value to the highest value.

However, it can be calculated by excel:

MEDIAN =MEDIAN (number 1, [number 2], …)

2. Interobserver agreement

In reading medical literature on diagnosis and interpretation of diagnostic tests, our attention is generally focused on items such as sensitivity, specificity and predictive values. These items address the validity of the test.

However, if the people who actually interpret the test cannot agree on the interpretation, the test results will be of little use. Therefore, Cohen's Kappa test is used in this calculation.

a. Cohen's Kappa test

Kappa test can be measured in any situation in which two neuroradiologist are evaluating the same thing.

Table A-1 Show table 2 x 2 for interpretation of two neuroradiologists

Epidemiology		**Neuroradiologist 1**	
		+	-
Neuroradiologist 2	+	a	b
	-	c	D

Calculation:

Kappa = (Observed - Expected) / (100 - Expected)

Observed agreement = 100 ×(a+d) / n; (n = a+b+c+d)

Expected by chance = 100 x (E1 + E2) / n

E1 = ((a+c)/n) × (a+b)

E2 = ((b+d)/n) × (c+d)

2.1. Interpretation of Kappa

Kappa	Agreement
< 0	Less than chance agreement
0.01–0.20	Slight agreement
0.21– 0.40	Fair agreement
0.41–0.60	Moderate agreement
0.61–0.80	Substantial agreement
0.81–0.99	Almost perfect agreement

3. Calculated statistic for accuracy of computer tomography

For the evaluation of clinical significant in diagnostic test may be table 2x2 by calculated TP, TN, FP, FN for PPV, NPV, specificity and sensitivity.

Definition of true positive (TP) is one that detects the condition when the condition is present.

Definition of true negative (TN) is one that does not detect the condition when the condition is absent.

Definition of false positive (FP) is one that detects the condition when the condition is absent.

Definition of false negative (FN) is one that does not detect the condition when the condition is present.

Table A-2 Show table 2 x 2 for calculation of accuracy

	Disease	No disease
Test positive	TP (a)	FP (b)
Test negative	FN (c)	TN (d)

Definition of positive predictive value (PPV) is the proportion of the examiner who is positive test and the presence of the condition. As, positive predictive value = [TP/(TP+FP)]x100.

Table A-3 Show table 2 x 2 for calculation of PPV

	Disease	No disease
Test positive	TP (a)	FP (b)
Test negative	FN (c)	TN (d)

Definition of negative predictive value (NPV) is the proportion of the examiner who is negative test and the absence of the condition. As, negative predictive value = [TN/(TN+FN)]x100.

Table A-4 Show table 2 x 2 for calculation of NPV

	Disease	No disease
Test positive	TP (a)	FP (b)
Test negative	FN (c)	TN (d)

Definition of sensitivity is measures the ability of a test to detect the condition when the condition is present. As, sensitivity = [TP/(TP+FN)]x100.

Table A-5 Show table 2 x 2 for calculation of sensitivity

	Disease	No disease
Test positive	TP (a)	FP (b)
Test negative	FN (c)	TN (d)

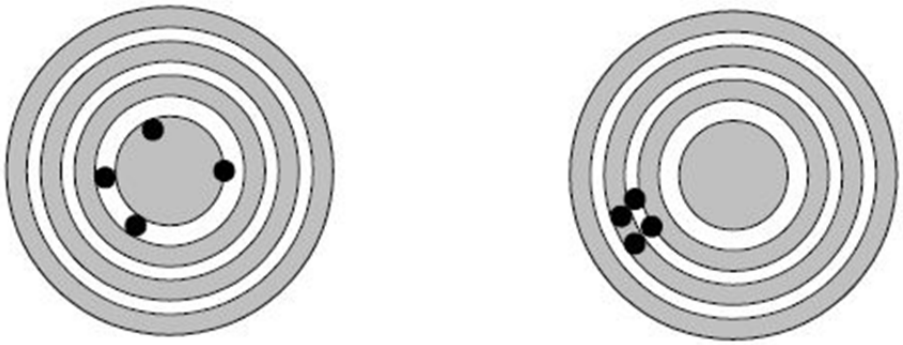
Definition of specificity is measures the ability of a test to correctly exclude the condition (not detect the condition) when the condition is absent. As, specificity = [TN/(TN+FP)]x100.

Table A-6 Show table 2 x 2 for calculation of specificity

	Disease	No disease
Test positive	TP (a)	FP (b)
Test negative	FN (c)	TN (d)

4. ACCURACY

Accuracy is a value that indicates to the ability of the instrument to read or measured values closer to reality. As, accuracy = [TP+TN/(TP+TN+FP+FN)]x100



High accuracy but low precision Low accuracy but high precision

Figure A.1 Show high accuracy and low accuracy

5. 95% CI calculator

A confidence interval (CI) expresses the precision of an estimate and is often presented alongside the results of a study (usually the 95% confidence interval). The CI shows the range within which we are confident that the true result from a population will lie 95% of the time. The narrower the interval, the more precise the estimate. There is bound to be some uncertainty in estimates because studies are conducted on samples and not entire populations. By convention, 95% certainty is considered high enough for researchers to draw conclusions that can be generalised from samples to populations. If we are comparing two groups using relative measures, such as relative risks or odds ratios, and see that the 95% CI includes the value of one in its range, we can say that there is no difference between the groups. This confidence interval tells us that, at least some of the time, the ratio of effects between the groups is one. Similarly, if an absolute measure of effect, such as a difference in means between groups, has a 95% CI that includes zero in its range, we can conclude there is no difference between the groups.

Table A-7 Show Table 2x2 for calculation of 95% CI

	Disease	**No disease**	
Test positive	TP (a)	FP (b)	$N_1 = a+b$
Test negative	FN (c)	TN (d)	$N_2 = c+d$
	$M_1 = a+c$	$M_2 = b+d$	$N = N_1 + N_2$

5.1 Calculation 95 CI of Sensitivity

$$SE_{Sen} = \sqrt{\frac{Sen\ (1 - Sen)}{\mathrm{m}_1}}$$

The 100(1-α) % confidence interval is defined as:

$$Sen - z_{1-\frac{\propto}{z}} SE_{Sen}, Sen + z_{1-\frac{\propto}{z}} SE_{Sen}$$

5.2 Calculation 95 CI of Specificity, $Spe = \frac{d}{m_2}$

$$SE_{Spe} = \sqrt{\frac{Spe(1 - Spe)}{m_2}}$$

The 100(1-α) % confidence interval is defined as:

$$\left(Spe - z_{1-\frac{\propto}{z}} SE_{Spe}, Spe + z_{1-\frac{\propto}{z}} SE_{Spe}\right)$$

5.3 Calculation 95 CI of Positive Predictive Value (PPV), $PPV = \frac{a}{n_1}$

$$SE_{PPV} = \sqrt{\frac{PPV(1 - PPV)}{n_1}}$$

The 100(1-α) % confidence interval is defined as:

$$\left(PPV - z_{1-\frac{\propto}{z}} SE_{PPV}, PPV + z_{1-\frac{\propto}{z}} SE_{PPV}\right)$$

5.4 Calculation 95 CI of Negative Predictive Value (NPV), $NPV = \frac{d}{n_2}$

$$SE_{NPV} = \sqrt{\frac{NPV(1 - NPV)}{n_2}}$$

The 100(1-α) % confidence interval is defined as:

$$\left(NPV - z_{1-\frac{\propto}{z}} SE_{NPV}, PPV + z_{1-\frac{\propto}{z}} SE_{NPV}\right)$$

APPENDIX B
CASE RECORD FORM OF CT FINDING FOR COMMON NEUROLOGICAL DISEASES IN HIV-PATIENTS

Date of study: .....

Sex: ( ) Male ( ) Female Age……years

CD4 count: ..... cells/mm^3

CT finding: ☐ Non- contrast enhancement

( ) Atrophy ( ) Hyperdense

( ) Isodense ( ) Hypodense

( ) Other.....

☐ Contrast enhancement

( ) Daughter sac ( ) Ring enhancement

( ) Nodular enhancement ( ) Patchy or Multifocal

( ) homogenous enhancement ( ) Leptomeningeal

( ) non-enhance ( ) Other.....

Location: ( ) Basal ganglia ( ) Thalamus ( ) Frontal lobe

( ) Parietal lobe ( ) Occipital lobe ( ) Temporal lobe

( ) Other.....

Distribution of lesion: ☐ Focal (≤ 3 lesion) ☐ Diffuse (> 3 lesion)

Number of lesion: ☐ Single lesion ☐ Multiple lesion ☐ Large lesion

Size of each Large lesion: 1st……cm.
2nd……cm.
3rd……cm.
Longest……cm.

Complication: ( ) Hydrocephalus ( ) Thrombosis ( ) Infarction

( ) Vasogenic edema ( ) Demyelination ( ) Herniation

( ) Mass effect ( ) Other……

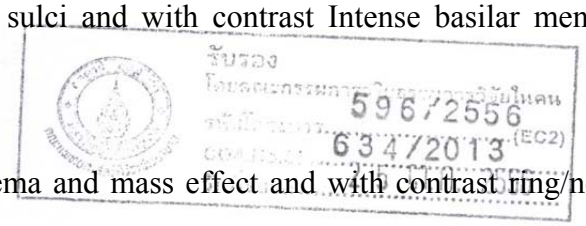
Criteria of Etiology:

( ) HIVE: normal or atrophy, hypodensity and no mass effect, CE non-enhancing

( ) Toxoplasmosis: multiple hypo-/isodense lesions with surrounding edema and mass effect and with contrast Thin, smooth rim or solid nodular enhancement

( ) PML: Multifocal, scalloping WM hypodense without mass effect or edema and with contrast non-enhancing

( ) TB meningitis: Isodense to hyperdense exudate effaces CSF spaces, fills basal cisterns, sulci and with contrast Intense basilar meningeal enhancement



( ) Tuberculomas: edema and mass effect and with contrast ring/nodular enhancing masses in cortex

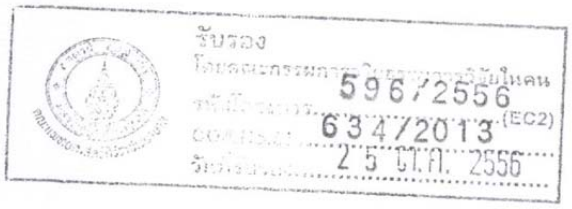
( ) Cryptococcosis: Solid or ring enhancing parenchymal mass with variable surrounding edema, located in close relation to the perivascular space. They may also arise within the choroid plexus a feature that can lead to an obstructive hydrocephalus

( ) PCNSL: Iso-,hyper- or hypodense and with contrast ring-shaped, irregular and sometimes homogenous or rim enhancement

Result of Etiology: ……

Image for printed ( ) Yes ( ) No No. of side……..

Sign……



แบบบันทึกประวัติข้อมูลและผลการวินิจฉัยของผู้ป่วยเอดส์ที่พบโรคทางระบบประสาท

ณ โรงพยาบาลศิริราช

1. ข้อมูลผู้ป่วย

รหัสผู้ป่วย ……เพศ.....อายุ.....ปี

เข้ารับการรักษาในวันที่…….....

ประวัติการได้รับเชื้อเอชไอวี

.....

.....

.....

.....

ผู้ป่วยติดเชื้อเอชไอวีอยู่ในระยะ.....

Surrogate markers (CD4 cells count).....cells/mm^3

โรคทางระบบประสาทที่พบ.....ชนิดเชื้อ.....

2. ลักษณะอาการทางระบบประสาท

.....

.....

.....

.....

แบบบันทึกประวัติข้อมูลและผลการวินิจฉัยของผู้ป่วยเอดส์ที่พบโรคทางระบบประสาท

ณ โรงพยาบาลศิริราช (ต่อ)

3. การวินิจฉัยโรคทางระบบประสาทในผู้ป่วยเอดส์

3.1. วิธีการตรวจทางคลินิก

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3.2. ผลการวินิจฉัยทางคลินิก

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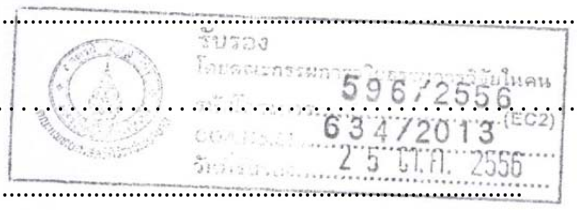

3.3. ผลการวินิจฉัยทางรังสี

.....

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.....

แบบบันทึกประวัติข้อมูลและผลการวินิจฉัยของผู้ป่วยเอดส์ที่พบโรคทางระบบประสาท

ณ โรงพยาบาลศิริราช (ต่อ)

สรุปผลการวินิจฉัยโรคทางระบบประสาทด้วยวิธีทางคลินิกและรังสีวินิจฉัย

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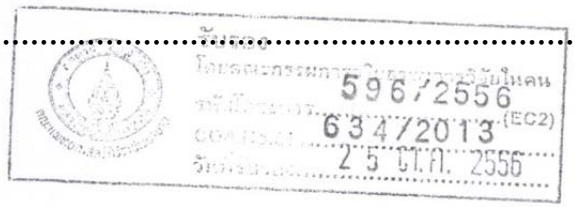

APPENDIX C

The SIRB approved the permission forms, Faculty of Medicine Siriraj hospital, Mahidol University.

2 ถนนพรานนก บางกอกน้อย
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โทรสาร +66 2411 0162

คณะกรรมการจริยธรรมการวิจัยในคน คณะแพทยศาสตร์ศิริราชพยาบาล
เอกสารรับรองโครงการวิจัย

หมายเลข Si 634/2013

ชื่อโครงการภาษาไทย : ความถูกต้องของภาพถ่ายเอกซเรย์คอมพิวเตอร์จากโรคทางระบบประสาทที่พบบ่อยในผู้ป่วยเอดส์ ณ โรงพยาบาลศิริราช

รหัสโครงการ : 596/2556(EC2)

หัวหน้าโครงการ / หน่วยงานที่สังกัด : รศ. นพ.พิพัฒน์ เชี่ยววิทย์ / ภาควิชารังสีวิทยา
คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล

สถานที่ทำวิจัย : คณะแพทยศาสตร์ศิริราชพยาบาล

เอกสารที่รับรอง :

1. แบบขอรับการพิจารณาจากคณะกรรมการจริยธรรมการวิจัยในคน คณะแพทยศาสตร์ศิริราชพยาบาล
2. โครงร่างการวิจัย
3. แบบบันทึกข้อมูล
4. ประวัติผู้วิจัย

วันที่รับรอง : 25 ตุลาคม 2556

วันหมดอายุ : 24 ตุลาคม 2557

คณะกรรมการจริยธรรมการวิจัยในคน คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล ดำเนินการให้การรับรองโครงการวิจัยตามแนวทางหลักจริยธรรมการวิจัยในคนที่เป็นสากล ได้แก่ Declaration of Helsinki, the Belmont Report, CIOMS Guidelines และ the International Conference on Harmonization in Good Clinical Practice (ICH-GCP).

ลงนาม .....
(ศาสตราจารย์ แพทย์หญิงชำรุพิมพ์ สูงสว่าง)
ประธานคณะกรรมการจริยธรรมการวิจัยในคน

- 4 พ.ย. 2556
.....
วันที่

ลงนาม .....
(ศาสตราจารย์คลินิก นายแพทย์อุดม คชินทร)
คณบดี คณะแพทยศาสตร์ศิริราชพยาบาล

- 5 พ.ย. 2556
.....
วันที่

Page 1 of 2

พิมพ์ที่หน่วยพิมพ์โรงพยาบาลศิริราช 2342 / 3,000 เล่ม / มิ.ย.55 / M / Mat.10023253

Figure C.1 The SIRB Certificate of Approval in Thai langue

2 PRANNOK Rd. BANGKOKNOI
BANGKOK 10700

Tel. +66 2419 2667-72
Fax. +66 2411 0162

Siriraj Institutional Review Board

Certificate of Approval

COA no. Si 634/2013

Protocol Title : Accuracy of CT for common focal neurological disease in HIV patients at Siriraj Hospital

Protocol number : 596/2556(EC2)

Principal Investigator/Affiliation : Assoc. Prof. Pipat Chiewvit, M.D. / Department of Radiology
Faculty of Medicine Siriraj Hospital, Mahidol University

Research site : Faculty of Medicine Siriraj Hospital

Approval includes :

1. SIRB submission form
2. Proposal
3. Case Record Form
4. Principle Investigator's curriculum vitae

Approval date : October 25, 2013

Expired date : October 24, 2014

This is to certify that Siriraj Institutional Review Board is in full Compliance with international guidelines for human research protection such as the Declaration of Helsinki, the Belmont Report, CIOMS Guidelines and the International Conference on Harmonization in Good Clinical Practice (ICH-GCP).

Jarupim Soongswang — 4 NOV 2013

(Prof. Jarupim Soongswang, M.D.) date

Chairperson

Udom K — 5 NOV 2013

(Clin. Prof. Udom Kachintorn, M.D.) date

Dean of Faculty of Medicine Siriraj Hospital

พิมพ์ที่หน่วยพิมพ์โรงพยาบาลศิริราช 2341 / 3,000 แผ่น / มิ.ย.55 / M / Mat.10023252

Figure C.2 The SIRB Certificate of Approval in English langue

2 ถนนวังหลัง บางกอกน้อย
กรุงเทพฯ 10700

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โทรสาร +66 2411 0162

คณะกรรมการจริยธรรมการวิจัยในคน คณะแพทยศาสตร์ศิริราชพยาบาล

เอกสารรับรองโครงการวิจัย (ต่ออายุ)

หมายเลข Si 634/2013

ชื่อโครงการภาษาไทย : ความถูกต้องของภาพถ่ายถ่ายเอกซเรย์คอมพิวเตอร์จากโรคทางระบบประสาทที่พบบ่อยในผู้ป่วยเอดส์ ณ โรงพยาบาลศิริราช

รหัสโครงการ : 596/2556(EC2)

หัวหน้าโครงการ / หน่วยงานที่สังกัด : รศ. นพ.พิพัฒน์ เชี่ยววิทย์ / ภาควิชารังสีวิทยา
คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล

สถานที่ทำวิจัย : คณะแพทยศาสตร์ศิริราชพยาบาล

เอกสารที่รับรอง :

1. แบบขอรับการพิจารณาจากคณะกรรมการจริยธรรมการวิจัยในคน คณะแพทยศาสตร์ศิริราชพยาบาล
2. โครงร่างการวิจัย
3. แบบบันทึกข้อมูล
4. ประวัติผู้วิจัย

วันที่ต่ออายุ (1): 25 ตุลาคม 2557

วันหมดอายุ : 24 ตุลาคม 2558

คณะกรรมการจริยธรรมการวิจัยในคน คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล ดำเนินการให้การรับรองโครงการวิจัยตามแนวทางหลักจริยธรรมการวิจัยในคนที่เป็นสากล ได้แก่ Declaration of Helsinki, the Belmont Report, CIOMS Guidelines และ the International Conference on Harmonization in Good Clinical Practice (ICH-GCP).

ลงนาม .....
(ศาสตราจารย์ แพทย์หญิงจารุพิมพ์ สูงสว่าง)
ประธานคณะกรรมการจริยธรรมการวิจัยในคน

21 ต.ค. 2557
.....
วันที่

ลงนาม .....
(ศาสตราจารย์คลินิก นายแพทย์อุดม คชินทร)
คณบดี คณะแพทยศาสตร์ศิริราชพยาบาล

22 ต.ค. 2557
.....
วันที่

Page 1 of 2

Figure C.3 The SIRB Certificate of Approval in Thai langue (Renewal)

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Tel. +66 2419 2667-72
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Siriraj Institutional Review Board

Certificate of Approval (Renewal)

COA no. Si 634/2013

Protocol Title : Accuracy of CT for common focal neurological disease in HIV patients at Siriraj Hospital

Protocol number : 596/2556(EC2)

Principal Investigator/Affiliation : Assoc. Prof. Pipat Chiewvit, M.D. / Department of Radiology
Faculty of Medicine Siriraj Hospital, Mahidol University

Research site : Faculty of Medicine Siriraj Hospital

Approval includes :

1. SIRB submission form
2. Proposal
3. Case Record Form
4. Principle Investigator's curriculum vitae

Renewal date (1st): October 25, 2014

Expired date : October 24, 2015

This is to certify that Siriraj Institutional Review Board is in full Compliance with international guidelines for human research protection such as the Declaration of Helsinki, the Belmont Report, CIOMS Guidelines and the International Conference on Harmonization in Good Clinical Practice (ICH-GCP).

Jarupim Soongswang — 21 OCT 2014

(Prof. Jarupim Soongswang, M.D.) — date

Chairperson

Udom K — 22 OCT 2014

(Clin. Prof. Udom Kachintorn, M.D.) — date

Dean of Faculty of Medicine Siriraj Hospital

Figure C.4 The SIRB Certificate of Approval in English langue (Renewal)

BIOGRAPHY

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